PREVENTION OF CONGENITAL DISLOCATION OF THE HIP JOINT IN SWEDEN

EFFICIENCY OF EARLY DIAGNOSIS AND TREATMENT

ACTA ORTHOPAEDICA SCANDINAVICA
SUPPLEMENT No 130
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A symposium held at the annual meeting of the Swedish Orthopaedic Association in Stockholm on April 5 1967

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Contents

Introduction

BY MAC FELLÄNDER

In 1912 LE DAMANY described a manoeuvre by which unstable hips in the newborn could be revealed (*segno de ressaut*). Many years elapsed before the important discovery led to early treatment of hip dislocation. ORTOLANI in 1935 was the first to use this abduction manoeuvre (*segno dello scatto*) as a clinical method of early diagnosis and to carry out systematic early treatment. For a long time little attention was paid to Ortolani's works both in Italy and elsewhere.

In Sweden PALMÉN introduced Ortolani's method in 1950 and soon succeeded in getting the National Board of Health to recommend in a circular letter of 1957 this method as a routine procedure for early diagnosis in all the maternity units in Sweden. Since then virtually all newborn babies are examined for hip dislocation. In a thesis of 1961 Palmén reported data from his own series as well as figures for the incidence in Sweden.

In 1952 VON ROSEN started systematic examination of newborn in the town of Malmö and he has published several reports of his results (1956, 1959 and later). His papers and his contributions in this field have received great attention in Sweden and in other countries.

Thus in Sweden we have now experiences from a 10-year period of nation-wide early diagnosis and treatment of unstable hips. The Swedish Orthopaedic Association believes that the time has come for discussing this question generally and has therefore asked for reports from some of those who have devoted special interest to these problems.

The symposium comprises submitted papers and contributions to the discussion as well as free discussion.

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Preluxation of the hip in the newborn

The diagnostic work in Sweden during the years 1953—1966

BY KURT PALMÉN FALKÖPING

As I was unable to accept the invitation to the symposium but was later asked to contribute to the discussion, I will first give a short account of the diagnostic work in Sweden. Since the beginning of the 1950's I have emphasized that the examination of the hip must be part of the routine examination of every newborn infant. I have then tried to follow these activities throughout the country and to study what effect the treatment of the newborn has had on the incidence of dislocation later treated in the orthopaedic departments. An account of the series up to and including 1960 will be found in my thesis published in Acta Paediatrica 1961. Since then the cases of hip dislocation from the orthopaedic departments, diagnosed after the newborn period, have been compiled for the years up to and including 1966. I will give some data from these series.

Diagnosis in the maternity departments

In 1953 examination of the hips was started at 26 obstetric departments with paediatric consultants and in 1956 examinations of the hips were performed at all the 45 departments with paediatric consultants. In 1962 a new drive was started to introduce the examination in all the small maternity units as well. In 1963 it was reported that examination of the hips of every newborn infant was made in 48 departments with paediatric consultants and in 55 smaller maternity units. About 110 000 or 99 %, of the newborn babies in Sweden were delivered in these hospitals. Less than 1 % were born at home.

Hip examinations and the incidence of preluxation in the newborn in Sweden from 1953–1963

	No. of infants born in departments where hips are examined	Percentage of all newborn in Sweden	No. of preluxation cases	Incidence of preluxation ‰
1953	33 000	31.0	32	1.0
1956	47 000	44.5	[illegible]	1.[illegible]
1959	[illegible]8 000	[illegible] 2	210	3.2
1960	[illegible]8 000	[illegible] 4	18[illegible]	2.[illegible]
1963	110 000	99.0	[illegible]	[illegible]

In the first years the incidence of diagnosed preluxation (the term "preluxation" will be used here; the cases of complete luxation in association with malformations are excluded) was about 1 per mill but had increased to 5.6 per mill in 1963. The incidence of "missed" cases was first higher but the high incidence for 1963 is in part very likely due to overdiagnosis. There would seem to be some geographical difference in the incidence for the whole country but figures of 15 to 20 per mill must be due to overdiagnosis. In the instructions for the technique of examination which were issued to the maternity departments in 1962 it was stated that only those cases in which the femoral head was clearly felt to be displaceable were to be recorded as "positive", whereas no significance was to be attached to snappings and crepitations. The overdiagnosis suggests that many examiners were too ambitious and perhaps too afraid of missing a case. Some babies who at the first examination in the maternity department had shown suspected symptoms which were not verified by the orthopaedist at examination a few days later were included and treated "for safety's sake".

Cases of dislocation "missed" in the newborn period

A survey of the cases of dislocation which were not diagnosed until *after* the newborn period and treated in all our orthopaedic departments shows a gradual decline of the incidence from about 110—120 cases each year before 1953 (83 % diagnosed after the age of one year) to about 35 each year between 1959 and 1961 with a further decrease to an average of 25 cases in the last four years from 1963 to 1966. By routine examination of the hips in the newborn and the prophylactic early treatment our cases of later dislocation have been reduced by about 80 % from the time before 1953.

Some cases are still missed at the examination in the maternity departments and to investigate the causes of this I have looked through the orthopaedic departments' records from 1962—1966 of cases of dislocation detected after the newborn period (here I wish to thank the heads of the departments for their kind permission). I will give some preliminary figures from this material (the survey is not yet completed).

127 cases of subluxation—luxation were not detected in the newborn period. So far it is known that out of 113 of these babies 56 were born in a department with a paediatric consultant service, 1 was delivered at home and the rest were born in smaller maternity units with no paediatric consultants.

As more than 80 % of the children in Sweden are born in departments with paediatric consultants the percentage of missed cases is much higher in the smaller units which lack paediatric consultants.

Out of the 127 cases 5 were cases of malformation arthrogryposis in 1

Preluxation of the hip in the newborn

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Hip examinations and the incidence of preluxation in the newborn in Sweden from 1953 to 1963

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1953	33 000	31.0	32	1.0
1956	17 000	11.[illegible]	78	1.[illegible]
1959	68 000	[illegible]2	21[illegible]	3.2
1960	68 000	[illegible]7.1	18	2.[illegible]
1963	110 000	99.0	61[illegible]	[illegible]

In the first years the incidence of diagnosed preluxation (the term pre luxation will be used here the cases of complete luxation in association with malformations are excluded) was about 1 per mill but had increased to 5 6 per mill in 1963 The incidence of missed cases was first higher but the high incidence for 1963 is in part very likely due to overdiagnosis There would seem to be some geographical difference in the incidence for the whole country but figures of 15 to 20 per mill must be due to overdiagnosis In the instructions for the technique of examination which were issued to the maternity departments in 1962 it was stated that only those cases in which the femoral head was clearly felt to be *displaceable* were to be recorded as positive whereas no significance was to be attached to snappings and crepitations The overdiagnosis suggests that many examiners were too ambitious and perhaps too afraid of missing a case Some babies who at the first examination in the maternity department had shown suspected symptoms which were not verified by the orthopaedist at examination a few days later were included and treated for safety s sake

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As more than 80 % of the children in Sweden are born in departments with paediatric consultants the percentage of missed cases is much higher in the smaller units which lack paediatric consultants

Out of the 127 cases 5 were cases of malformation arthrogryposis in 1

myelomeningocele in 1, myelomeningocele combined with club foot in 1 and club foot in 2.

Out of 97 babies with known birth-weight 14 were prematures, which is about three times the normal proportion of prematurity. In the group of newborn with preluxation, on the other hand, the proportion of prematures was not increased. The probable explanation for the high incidence of prematures may be that many of the premature babies are immediately transferred to a ward for prematures or to a paediatric department and placed in an incubator, and their hips are not examined. The same explanation would be valid for a further two or three babies in the series who were immediately transferred to an infant ward because of asphyxia and who were in poor condition for a few days.

An interesting observation is that in five infants preluxation was suspected at the examination in the maternity department but X-ray was reported to have been negative; these infants were therefore left untreated. Dislocation was detected later, in two of them not until their second year.

Thus in most cases it is probably the "human factor" that can be blamed for the failure of detecting dislocation at the examination in the newborn period. If congenital dislocation is not to be missed in the newborn, the following measures would be important:

To make a careful clinical examination of the hips in every newborn infant, not to forget those who immediately after birth are transferred to wards for prematures, infant wards, etc., and those born at home;

to give special attention to the hips in cases of malformation, especially of the bones and joints, such as arthrogryposis, myelomeningocele, dislocation of the knee-joint, and club foot;

not to rely upon a negative X-ray examination.

X-ray examination of the newborn

Preluxation in the newborn is a condition in which subluxation can be manifest when the leg is held, for instance, flexed, adducted but reduction occurs when the leg is flexed and abducted to 80–90°. As I pointed out in 1961, the X-ray examination must be made with the baby's leg held in such a position that the examiner can feel that the head of the femur has been displaced (I disregard the cases of malformation with complete luxation) and much depends here upon the assistant who holds the baby during the examination. It is also important to ensure an exactly symmetrical position of the pelvis, since any rotation from one side to the other or different degrees of lordosis will greatly influence the acetabular angle. I am not yet convinced that the X-ray examination provides any information in

addition to the clinical examination and believe that it can be omitted in the practical diagnosis of hip dislocation in the newborn

It is also obvious that errors can easily be made Among the infants with dislocation referred to the orthopaedic departments between 1953 and 1966 I have found no less than 35 who showed clear or suspected symptoms in the new born period but who were left without treatment because of negative X ray—and without careful checkings

X ray examination later on at the age of 5 or 6 months (earlier if there is a suspicion of subluxation) to check the effects of treatment and thereafter at for instance the ages of 1 and 3 years may be justifiable in order to follow the growth of the capitular nucleus and the acetabular roof

Treatment

Does every newborn infant with signs of preluxation need treatment and for how long? The displaceability of the femoral head and the click disappear within the first week of life in many cases within one or two days of birth in some cases This means that the incidence will probably be higher if the examination of the newborn is made on the first day than on the third or fourth day of life We know that there will be a normal hip development without treatment in many of these cases various authors estimate these mild cases at about 30 % In some instances in which the baby lay with its legs flexed and abducted to 80—90 I postponed treatment for a few days If the symptoms had disappeared by then I left the baby untreated In other cases in which the baby tended to lie with its legs more adducted I applied a bandage which was removed after one or a few days If by then the hip was stable at an attempt to displace the femoral head the bandage was not re applied The babies who had no or very short treatment were observed particularly carefully for the first few months In a few cases the treatment had to be re started but in the rest of these mild cases the hips developed quite normally In infants with very marked displaceability and hip laxity I extended the treatment to about one month—lately seldom longer

The short term treatment was used for the sake of trial and is not of course to be recommended as a practice to be followed generally But I do believe that expectancy is justifiable in the mild cases in which displaceability of the femoral head is noted at examination on the first or second day of life but has disappeared when the baby is examined a few days later In some clinics abroad they do not treat infants in whom the clinical symptoms disappear within the first week of life and consider that this policy works satisfactorily

myelomeningocele in 1 myelomeningocele combined with club foot in 1 and club foot in 2

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Instability of the hip in the newborn

Fifteen years experiences in Malmo

BY SOPHUS VON ROSEN MALMO

I presume that you are all more or less acquainted with the principles of diagnosis and treatment that have for many years been used at the department of orthopaedic surgery Malmo General Hospital and will therefore confine my paper to a few remarks and mainly on the results of treatment

The long term results are largely what I reported at the meeting of SICOT in Paris in September 1966 The material consists of all cases treated at Malmo in the years 1952—1960 and after-examined in 1965—1966 Of the some 21 000 infants born at the department of obstetrics in Malmo instability of the hip was diagnosed in 38 new borns with all together 68 unstable hips The duration of follow up is given in Table 1

At the after-examination the following clinical and roentgenological observations were made

Clinically all the children except two were symptom free One of these was a girl who from 12 months of age had developed spastic paraplegia with consequent defective abduction and reduced range of motion of both hips The other was a 12 year old girl who complained of weakness of one of the hips (Fig 1 b)

Roentgenologically the children were examined for

a) poor development of the acetabulum with subluxation and/or

b) Perthes-like changes of the femoral head

a) *Poor development of the acetabulum with subluxation*

Apart from the above case with paraplegia two hips showed subluxation of the femoral head The subluxation of one of these was only slight (Fig 1 a) The other hip was the one which felt weak on exertion Here roentgen exam

Table I Ages of Thirty six Children Re examined

Age in years	Number
6—9	25
9—13	11

Secondary bone changes

As regards the *secondary bone changes* discussed at the symposium much is still unclear. In some respects such changes probably depend upon the treatment and the time at which it is started. If treatment is started within the first week of life secondary bone changes develop very seldom. In the earlier part of my own series which now comprises about 130 infants there were *two cases of necrosis of the head and a few of slight dysplasia*. *Among* about 50 cases from 1961—1967 there were two of dysplasia which persisted at the age of two or three years.

The short-term treatment that I have tried for the last eight years was designed partly to study potential bone changes. The results are not yet ready for publication but I hope to be able to present them shortly.

Summary

In Sweden since 1953 hip examination is a routine at the obstetric departments. In the last years almost every newborn is examined (more than 99 % are born in hospitals). The incidence of diagnosed preluxation is about 5 per mill (there are still some overdiagnosis).

Thanks to this diagnostic work and the immediate treatment of the new born the cases of later dislocation have been reduced from 110—120 cases yearly before 1953 to 25 in the last years. Still some cases are missed in the newborn most of them owing to the human factor.

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In Sweden since 1953 hip examination is a routine at the obstetric departments In the last years almost every newborn is examined (more than 99 % are born in hospitals) The incidence of diagnosed preluxation is about 5 per mill (there are still some overdiagnosis)

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were unstable immediately after birth and that in each child one hip soon became stable despite the inadequate treatment

b) *Perthes like changes of the femoral head*

In none of the children were any Perthes-like changes of the femoral head observed Only in one case did one side show a slight shortening and thickening of the femoral neck (Fig 1 c) Also that case belonged to the first eight Treatment was started when the child was three weeks old and the hip in question remained unstable for eight months The development of the other hip which was also originally unstable was normal

Comments on diagnosis

The following questions deserve special attention

a) Table II shows the *frequency of diagnosed cases* during a 10 year period (1956—1965) The frequency varied considerably from year to year I cannot offer any satisfactory explanation for this variation During the entire period the children were examined by the same team of paediatricians at the department of obstetrics and by the same roentgenologists and by the same orthopaedists

A certain increase may be partly explained by the fact that during this period it was gradually realised how important it is to diagnose the condition early if satisfactory results are to be obtained with the consequence that all newborns were examined still more carefully Another possible contributory reason is the increasing number of immigrants to Malmo from Jugoslavia Italy and other Mediterranean countries

b) *How many cases of instability of the hip have remained concealed at the*

Table II The Incidence of Congenital Instability of the Hip in Live Births in Malmo 1956—6[illegible]

Year	Number of cases	Per cent
[illegible]	4	0 13
	5	0 16
	[illegible]	0 3[illegible]
		0 21
		0 [illegible]8
		0 53
		0 2
		0 [illegible]7
		0 6[illegible]
		1 [illegible]9



Fig 1 The three girls in the long term follow up who did *not show quite normal X rays all of them treated before* we developed our present routine treatment a Slight subluxation left side b Marked subluxation right side c Slight shortening and thickening of the right femoral neck

ination showed a wide acetabulum with a sloping roof and marked subluxation of the femoral head (Fig 1 b) Both cases belonged to the first eight we had treated *i e* before we had obtained sufficient experiences and above all before we had realised that the femoral head must be held in reduced position *continuously* from the very beginning of treatment if the desired result is to be achieved In both cases the mothers found the treatment troublesome and occasionally removed the abduction bandage then used The result was that these hips did not become stable until the children were about 1 year old It should be mentioned that in both cases both hips

were unstable immediately after birth and that in each child one hip soon became stable despite the inadequate treatment

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Year	Number of cases	Per cent
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1958	12	0 37
1959		0 21
1960	9	0 28
1961	18	0 53
1962	9	0 2[illegible]
1963	[illegible]9	0 [illegible]
1964	26	0 65
1965	5[illegible]	1 [illegible]9



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1958	12	0.37
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1960	9	0.28
1961	18	0.53
1962	9	0.27
1963	9	0.27
1964	26	0.65
1965	52	1.29



Fig 2 The first case missed at the routine examination at the maternity dept A left sided dislocation indicated by the fact that the child limped when starting to walk was diagnosed at the age of 14 months Closed reduction was performed resulting in a persistent subluxation at the age of 11 years

department of obstetrics? Four all in girls in 1956 1960 1963 and 1966 respectively The first case was discovered by the fact that the child limped when she began to learn how to walk (Fig 2 a) The parents were living elsewhere and the child was treated there with closed reduction and a plaster cast Treatment appeared to offer no difficulties but the result was subluxation (Fig 2 b) The reason why this case was missed at the department of obstetrics might be that the child had asphyctic convulsions the day after birth and was therefore transferred to another department

The second and third cases were also betrayed by a limp when the children began to walk in the beginning of the second year of life (Figs 3a and 4a) Both were treated at the department of orthopaedics in Malmo with closed reduction and Lorenz cast (plaster) in one case combined with adductotenotomy The results obtained were satisfactory in both cases (Figs 3b and 4b)



Fig 3 The second case missed at the routine examination at the maternity dept X ray at the age of 17 months showed a dislocation clinically indicated by a limp on the left side After closed reduction and adductortenotomy the joint has developed satisfactorily

It is not known why these cases were missed at the department of obstetrics it must presumably be ascribed to the so-called human factor

The fourth case was manifested by impaired abduction of both hips The child was then one month old Roentgen examination showed bilateral dislocation of the hip (Fig 5) Treatment has proved difficult and is not yet concluded The reason why this case was missed may have been that the femoral head might have been so highly dislocated already at birth that on manipulation it did not reach the same level as the lip (edge) of the posterior part of the acetabulum with the result that it was not possible to produce the reduction click This assumption is strengthened by observations in another one of our cases At examination at the department of obstetrics some slight atypical clicks of one of the hips were perceived in this case To make





Fig. 4. The third case missed at the routine examination at the maternity dept. When the girl started to walk at the age of 17 months there was a limp on the left side. Closed reduction was easily performed and the hip has developed satisfactorily.

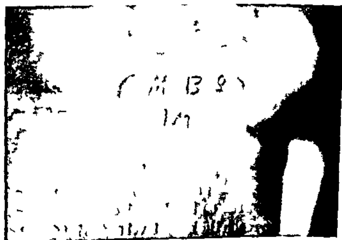


Fig. 5. The fourth case missed at the routine examination at the maternity dept. at the age of one month. A high dislocation on both sides, manifested by limitation of abduction, was discovered at a routine examination in the postnatal clinic.

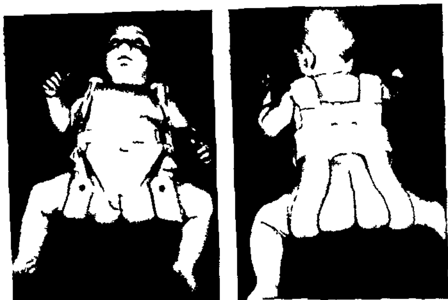


Fig. 6. A larger model of our frame, strengthened by straps, is recommended for strong and lively babies in order to prevent them from wriggling the legs out of the frame.

sure the child was referred to the roentgen department. Examination there revealed bilateral high luxation dislocation. Both hips could be reduced without difficulty and routine treatment resulted in a normal development of the hips.

Comments on treatment

Since 1956 all diagnosed unstable hips have been treated with the abduction frame constructed at the department of orthopaedics in Malmö. In my opinion the advantages of this frame are that when properly applied it holds the hips in reduced position and, secondly, it can be worn when the child is being washed and, thirdly, treatment of the child can without any difficulty be managed by the mother. The child is re-examined every 2—3 weeks at the outpatient department of orthopaedics, where the frame is removed and the child is given a bath. Originally the appliance was made in only one size but now somewhat larger and smaller models are also available. One should take care that strong and lively children do not wriggle one or both legs out of the frame. In such cases, which are uncommon, the legs can be held more firmly in the frame by application of a few straps on the frame (Fig. 6).

The children's age at beginning of treatment during the 10-year period (1956–1965) are given in Table III.

The duration of treatment during the same period is given in Table IV.



a



b

Fig. 4. The third case missed at the routine examination at the maternity dept. When the girl started to walk at the age of 17 months there was a limp on the left side. Closed *reduction* was easily performed and the hip has developed satisfactorily.



Fig. 5. The fourth case missed at the routine examination at the maternity dept. at the age of one month. A high dislocation on both sides, manifested by limitation of abduction, was discovered at a routine examination in the post natal clinic.




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The children's age at beginning of treatment during the 10-year period (1956–1965) are given in Table III.

The duration of treatment during the same period is given in Table IV.



Fig. 7. The last X-rays of a girl at the age of 6 years, which revealed an unusual degree of instability of the hips and of the pelvic junctions at birth. In spite of routine treatment in our frame followed by plaster for [illegible] months the left hip remained unstable up to the age of 10 months. The girl is clumsy, with gynecomastia, and an endocrine disorder is suspected.

Of the eight cases treated for more than 3 months, four were treated f[…] up to 1 months, during the last month mainly only during the night. T[…] of the remaining four were the first to be treated with our newly constructe[…] frame. At that time we were not sure how long the frame should be worn.

The case treated with plaster is of particular interest.

The patient was a girl with highly marked instability of the hips as wel[…] as of the pelvic joints. We had begun to wonder whether it was really nece[…] sary to keep the child in the frame for such a long period as three months, an[…] since both hips felt stable after 3 weeks the frame was removed. At follow u[…] three weeks later the right hip was still stable, but the other one was ve[…]

Table III. Ages at the beginning of Treatment (1956–6[illegible])

Age in days	Number of cases
1–2	45
3–4	10
5–6	[illegible]
Total	[illegible]

Table IV. Duration of Treatm[…] (1[…])

Month	Number of c[…]
Up to 1	1
Up to 2	[illegible]
Up to 3	[illegible]
More than 3	
Total	

Up to 4 month
With plant [illegible] model
Early plaster [illegible]

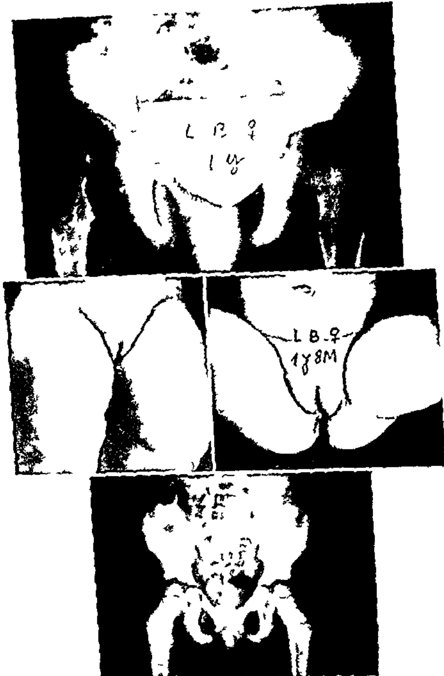


Fig. 8. A 1 m... t ks girl with bilateral instability in the hips at birth treated in our position way. Both hips became stable *within three* months. At a follow up at the age of 10 months the right hip was unstable *again with incipient* dysplasia of the acetabular *roof*. After 8 months treatment in a larger *model of our frame* the hip became stable and has developed normal. The general configuration of the girl became more normal.

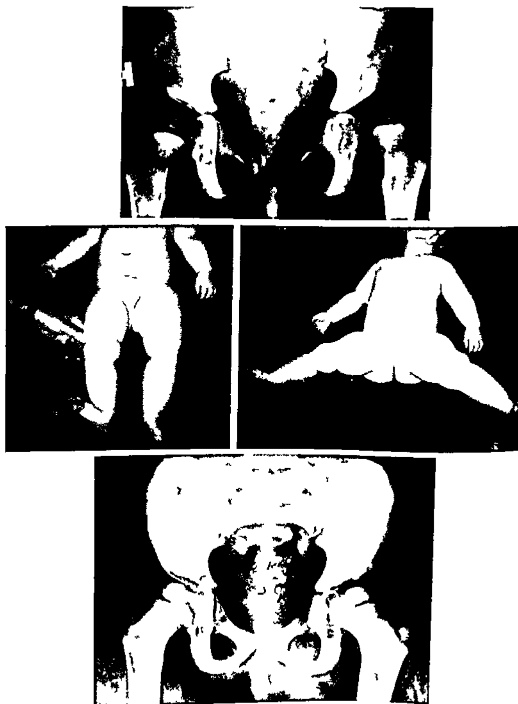


Fig 9 Another clumsy baby girl with hypermobile joints and bilateral instability in th[illegible] hips at birth With our routine treatment both joints became stable in th[illegible] reduced posi tion within three months At a routine follow up at the age of 12 m[illegible] the left hi[illegible] was unstable again and X rays revealed dysplasia of the acetabular roof A[illegible]r 4 month[illegible] of renewed treatment in our frame the hip became stabl[illegible] and th[illegible]ular roof developed satisfactorily The general configuration of the girl is now [illegible]mal



Fig 10 X ray of a recently treated girl with marked heredity for C.D H a cousine of the girl shown in fig 8 Both hip joints were highly unstable at birth In spite of routine treatment for three months the right hip remained unstable A plaster of Paris was applied for one month followed by a larger model of our frame up to the age of 9 months The joint became stable and now seems to develop normaly There is a general hypermobility in all joints but otherwise the body build is quite normal

unstable and remained so for 10 months despite immobilisation in plaster from 1 to 10 months of age Both hips afterwards developed in a normal way (Fig 7) This girl has always been and still is rather clumsy and her joints are hypermobile Some sort of endocrine disorder is suspected because of inter alia gynecomastia

An unusually crude body build and general hypermobility of the joints was also noted in the only two cases with recurrent instability of the hips both after primarily successful routine treatment At the routine follow up of these girls at the age of 10 and 12 months respectively instability of one of the hips was noted with dysplastic acetabulum on the same side Both girls were placed in a larger model of the frame one for 8 months and the other for 4 months When last examined roentgenologically the hips appeared practically normal The outer shape had also become normal (Figs 8 9)

The last case in which the course of treatment deviated from that in the others was strangely enough one of my grand nephews who was born in December 1966 with high severe instability of both hips preponderantly on the right side There is a strong hereditary on the maternal side The maternal grandmother and maternal aunt have dislocation of the hip and the child s cousin is one of the above-mentioned cases with recurrent instability Treatment was started in the usual way and the left hip became stable after 6 weeks treatment But the right hip was still unstable after 3 months and roentgen examination showed signs of acetabular dysplasia The hip

was recently placed in Lorenz plaster and I hope and believe that also this hip will become stable and develop normally. The child has hypermobile joints but is of otherwise normal body build.[1]

Summing up I believe that this method of treatment devised by us is adequate but one should be on the watch for children with crude body build and hypermobile joints and also for children with hereditary predisposition. It is possible that our treatment was somewhat too rigorous and that some of the children might not have required any treatment at all. On the other hand treatment does not entail any real inconvenience and has never had any undesirable effect.

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Radiography of the hip joint in the neo-natal period

Demonstration of X-ray pictures

BY LARS ANDRÉN MALMÖ

Reference

Andrén, L. (1962). *Pelvic instability in newborns.* Acta Radiol. Suppl. 212.

[1] Two years have elapsed since then. After 1 month in plaster the right hip was stable and reduced and the plaster was replaced by a larger model of our frame. This was removed when the child was 3 months old. The child began to walk at 11 months and has run about in a normal way. Roentgenologically the left hip is normal and the right hip has grad[illegible] [illegible]factory way. On both sides development of the bone nucl[illegible] [illegible]ied (Fig. 10).

Result of treatment from birth of unstable hips

A 5 year follow up

BY CARL HIRSCH & SVEN SCHELLER GÖTEBORG

Introduction

In the early fifties Palmén and Selander pediatricians at different children's hospitals in Sweden started to examine all newborn for dislocation of the hips. Since practically all children in Sweden, in 1958 98.9 per cent, are delivered in maternity wards a great number of new born were referred to orthopaedic departments the first days of life when Ortolani's phenomenon or only unstable hips explained as slack joint capsules had been noticed. Many previous reports had convincingly illustrated that early abduction treatment of congenital hips led to anatomical normalization (Putti 1929, 1933, Frölich 1932, Hilgenreiner 1935, Frejka 1941, Hart 1950). The interest for immediate care grew rapidly throughout this country encouraged by von Rosen (1956), Palmén (1961), Andrén (1962). Long term follow ups of closed reduction by the method of Lorenz (1920) have been presented by Wiberg (1939) and Severin (1941) illustrating the inefficiency of this treatment and the number of problems at later age. It is therefore imperative to investigate the development of early treated hips in which at the time of management very few really had a dislocated joint but rather something that was felt indicative of C.D.H. The purpose of this presentation is to report the present results of the children born in Göteborg in 1961 and 1962.

Material

In Göteborg all children are delivered in two maternity clinics. Each child is examined during the first day of life with regard to hip-joint stability. The frequency of unstable hips in Göteborg was in 1961 for boys 6/3077 (0.[illegible] per cent) and for girls 32/30[illegible]2 (1.1 per cent). In 1962 the rate was in boys [illegible]/3210 (0.2 per cent) and in girls 19/2971 (1.7 per cent). Arthrogrypotic infants were not included.

In these 93 infants 123 hips were unstable, 30 were bilateral and 63 unilateral, 31 on the left and 32 on the right side.

Roentgenograms were taken in all these children. Radiographic indications of congenital hip dysplasia and dislocation were defined with regard to mean and pathologic values at time of birth. 25 hips were considered

was recently placed in Lorenz plaster and I hope and believe that also this hip will become stable and develop normally The child has hypermobile joints but is of otherwise normal body build [1]

Summing up I believe that this method of treatment devised by us is adequate but one should be on the watch for children with crude body build and hypermobile joints and also for children with hereditary predisposition It is possible that our treatment was somewhat too rigorous and that some of the children might not have required any treatment at all On the other hand treatment does not entail any real inconvenience and has never had any undesirable effect

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Radiography of the hip joint in the neo natal period

Demonstration of X ray pictures

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Reference

Andrén L (1962) Pelvic instability in newborns Acta Radiol Suppl *212*

[1] Two years have elapsed since then After 1 month in plaster the right hip was stable and reduced and the plaster was replaced by a larger model of our frame This was removed when the child was 9 months old The child began to walk at 11 months and has since run about in a normal way Roentgenologically the left hip is normal and the right hip has gradually developed in a satisfactory way On both sides development of the bone nucleus in the femoral epiphysis is retarded (Fig 10)

Result of treatment from birth of unstable hips

A S y r f ll w up

BY CARL HIR CH & SVEN SCHELLER GOTEBORG

Introduction

In the early fifties Palmen and Selander pediatricians at different children s hospitals in Sweden started to examine all newborn for dislocation of the hips Since practically all children in Sweden in 1958 98 9 per cent are delivered in maternity wards a great number of new born were referred to orthopaedic departments the first days of life when Ortolani s phenomenon or only unstable hips explained as slack joint capsules had been noticed Many previous reports had convincingly illustrated that early abduction treatment of congenital hips led to anatomical normalization (Putti 1929 1933 Froelich 1932 Hilgenreiner 1935 Frejka 1941 Hart 1950) The interest for immediate care grew rapidly throughout this country encouraged by von Rosen (1956) Palmen (1961) Andren (1962) Long term follow ups of closed reduction by the method of Lorenz (1920) have been presented by Wiberg (1939) and Severin (1941) illustrating the inefficiency of this treatment and the number of problems at later age It is therefore imperative to investigate the development of early treated hips in which at the time of management very few really had a dislocated joint but rather something that was felt indicative of CDH The purpose of this presentation is to report the present results of the children born in Goteborg in 1961 and 1962

Material

In Goteborg all children are delivered in two maternity clinics Each child is examined during the first day of life with regard to hip-joint stability The frequency of unstable hips in Goteborg was in 1961 for boys 6 3077 (0 2 per cent) and for girls 32 3002 (1 1 per cent) In 1962 the rate was in boys 6 3210 (0 2 per cent) and in girls 49 2971 (1 7 per cent) Arthrogryposis infants were not included

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[1] Two years have elapsed since then. After 1 month in plaster the right hip was stable and reduced and the plaster was replaced by a larger model of our frame. This was removed when the child was 3 months old. The child began to walk at 14 months and has since run about in a normal way. Roentgenologically the left hip is normal and the right hip has gradually developed in a satisfactory way. *On both sides development of the bone nucleus in the femoral epiphysis is retarded* (Fig. 10).

Result of treatment from birth of unstable hips

A 5 y a f ll w up

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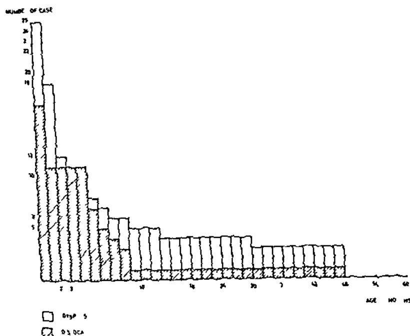
dysplastic or luxated e g 20 per cent of the total number of unstable joints *The incidence of radiographically visible changes were in 1961 amongst boys* 0 03 per cent and girls 0 1 per cent In 1962 the figures were 0 06 and 0 3 respectively

It is hard to tell if those hips which already at birth show evidence of CDH are the only ones to develop a real dislocation if not treated immediately and how many of the radiographically normal hips with clinical signs of instability with or without *Ortolani clicks will cause acetabular* disturbances and different degrees of joint malformations *It is quite obvious that at least* some unstable hips will be normal very soon even if no treatment is given The degree of instability varies It is most pronounced the first day of life Some will be stable if reexamined a few days or a week later In this study only those were treated where the orthopaedist was able to confirm the findings of the pediatrician both seeing the patient within a day or two

In order to have some idea of the difference in frequency of dislocations a comparison was made between children born in 1951—55 when early treatment was not completely organized and in 1961—62 when all new born were compulsorily checked Since the orthopaedic department is the only hospital in Goteborg where the citizens can bring their children if hip involvement is recognized they will turn up sooner or later Everyone born in 1951—55 regardless of when he or she was admitted for hip disorder was checked Those with a diagnosis of CDH were recorded Naturally in this way children with asymptomatic dysplasia or subluxation escaped our efforts The frequency of congenital dislocations of hips based on radiographic evidence in *1951—55 and in 1961—62 were compared The incidence* was somewhat higher when control at the time of birth was effective

Even if such a comparison may speak in favour of early roentgenograms in order to find the really severe hips it is obvious that many of the unstable hips will during the radiographic examination lie in a normal position Attempts have been made to take X rays while the femoral head is forced out of its position In this way some more may be regarded as positive findings but there will still be the majority showing normal roentgenograms *Many of these may nevertheless be potential dislocations A slack capsule* allowing the femoral head abnormal motion in the acetabulum may affect the anatomical shape of the joint (Langenskiold & Sarpio 1957 Wilkinson 1963 Stanisavljevic & Mitchell 1963) We therefore decided to treat all children with unstable hips in abduction In doing so however we did take into consideration the question whether such a joint position might effect the development of the joints whether or not it could harm the epiphysis Radiograms have been taken at 3 months one year two years and at four five years of age

Radiographic normalization of hip dislocation and dysplasia following early abduction treatment



Treatment

Most of the children were splinted in a Frejka type of pillow a few received the aluminium frame of von Rosen or Palmen The time in abduction varied In general they were kept 2—4 months During this period they were checked several times in the out patient department If the radiograms did indicate dysplasia or luxation they remained in abduction longer Eventually a plaster of Paris (double hip spica) was made

Results

At one year of age 89 of the 93 children showed radiographically normal hip-joints One year later one more child had a normal joint At age four two children showed very mild dysplasia and in one joint there was only a small difference in the levels of the epiphyseal bone centres in the diagram indicated as dislocation (Fig) At age five all these children had normal hip-joints

No radiographic changes have remained in the femoral epiphysis indicating that early abduction is harmful Delayed development of the epiphyseal bone centre is quite common on the affected side but becomes normal some months later and remains normal

Summary

The frequency of unstable hips in new-born in Goteborg was in 1961 0? per cent for boys and 1 1 per cent for girls in 1962 0 2 and 1 7 per cent respectively One third was bilateral one third affected the right and the same proportion the left hip-joint 20 per cent showed radiographic indications of dysplasia or luxation

All infants were treated in abduction immediately With few exceptions a Frejka type of dressing was used in general during two four months The children were all checked at intervals radiographically Within one year 96 per cent (89/93) had completely normal hip-joints A year later one more child had developed a normal hip At age four two children still showed evidence of mild dysplasia and one hip was slightly subluxated At age five these three hips were normal

As a rule the femoral epiphyseal bone centre developed later on the affected side No signs of disturbances occurred After the epiphyseal bone centre had become equal sized it remained normal

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Analysis of a material of congenital dislocation of the hip[1]

BY U. JAMES AND J. A. SEVASTIKOGLOU, UMEÅ

The present paper concerns an analysis of a series of congenital dislocations of the hip (CDH) observed in the Department of Orthopaedic Surgery, University Hospital, Uppsala, in children born during the years 1962 to 1965.

Besides typical cases of congenital dislocation of the hip—preluxation (Palmén 1961)—the series includes some atypical cases, such as dislocation combined with other congenital malformations (e.g. arthrogryphosis and myelomeningocele).

Material

The patients. As demonstrated in table I, altogether 373 children born between 1962 and 1965 were referred to the Department because of diagnosed or suspected CDH.

The material is divided into two groups: newborn, 255 cases referred before 2 weeks of age, and infants, 118 cases referred after 2 weeks of age. Of the total number, 90 were boys and 283 girls, the ratio for both groups being approximately 1:4.

Table I. The material

	No. of newborn referred before 2 weeks of age	No. of infants referred after 2 weeks of age	Total	Total load
Girls	194	89	283	
Boys	61	29	90	373
Delivery in the University Hospital	242	53	295	
Delivery in other hospital	13	65	78	373

[1] Part of the present material has been published by T. Hiertonn and U. James, Uppsala (J. Bone Joint Surg. 50 B, 542–545, 1968).

From the Department of Orthopaedic Surgery, University Hospital, Uppsala, Sweden. Head: Prof. T. Hiertonn, M.D.

The distribution of the patients by the age at which they were referred and first examined in the Orthopaedic Department is shown in table II More than 88 per cent or 214 of the newborn were examined during the first week of life 87 per cent or 103 infants were admitted to and examined in the Orthopaedic Department during their first year 242 newborn and 53 infants were born in the maternity ward of the University Hospital and 13 and 65 respectively in maternity wards of other hospitals in the Uppsala region

Diagnosis The hips of all the children born in the University Hospital were examined in the maternity ward by a consultant paediatrician Children born at other hospitals were examined in the maternity ward either by the surgeon in charge or by a consultant paediatrician All the children were later examined on several occasions at the children s welfare centres by paediatricians or general practitioners Every child in whom abnormality of the hips was diagnosed or suspected was immediately transferred to the Department of Orthopaedic Surgery at the University Hospital where a second examination was performed by one of the senior members of the staff

The diagnosis in the newborn was always based on clinical findings such as Ortolani s click positive provocation test by Palmen s technique decreased abduction of the hip apparent shortening of the leg and suspected crepitations X ray examination was performed in the newborn in exceptional cases only

Treatment and results Among the total number of children admitted to the Department 13 newborn and 69 infants were assessed as completely normal and not in need of treatment The remaining 291 received one of three different types of treatment as shown in table III

Newborn The standard treatment was by abduction in a splint almost exclusively of the Frejka pillow type usually for three months No complications were observed in any of the cases thus treated A small number of newborn altogether 10 babies received special treatment either with plaster in abduction position or by closed reduction because of persistent dislocation

Table II Age and number of children at first examination in the Department of Orthopaedic Surgery Uppsala

Age in days No of newborn	1 6	2 30	3 3	4 53	5 30	6 38	7 25	8 10	9 10	10—14 8	Total 24[illegible]
Age in months No of infants	[illegible]—1 7	1—3 27		3—6 40		6—12 29		12—24 10		24	 118

Only children born in the maternity department of the University Hospital are included

Among the newborn who received special treatment 7 were born at the University Hospital Five of them had typical CDH and two atypical CDH (myelomeningocele and arthrogryphosis)

In 1 of these latter cases the reason for special treatment was a slight acetabular dysplasia diagnosed at the regular three month checkings After a period of prolonged abduction treatment in plaster the hips of these babies developed satisfactorily

In the other 3 cases (2 typical and 1 atypical) the dislocation persisted in spite of primary treatment by means of a Frejka pillow

In the first case dislocation of one hip and subluxation of the other were diagnosed on the third day after birth The baby was treated with a Frejka pillow for 8 weeks but dislocation persisted Closed reduction was therefore performed and a plaster cast was applied for a further 8 months The development was then very satisfactory In the second case laxity of one hip with Ortolani s click was diagnosed on the fifth day after birth The baby was placed in a Frejka pillow for 2 months The X ray examination 5 months later showed however dysplasia of the acetabulum with subluxation of the femoral head Closed reduction was therefore performed and a plaster cast was applied for 7 months The development of the hip was then very satisfactory The third case (the atypical one) occurred in a baby with arthrogryphosis in whom dislocation of both hips was diagnosed the fifth day after birth Traction of the hips was applied for some days and closed reduction was then attempted but the result was not satisfactory After open reduction of both hips and prolonged immobilization in plaster a very satisfactory result was obtained

Infants Out of the 118 infants between 2 weeks and 2 years old referred to the Department of Orthopaedic Surgery because of diagnosed or suspected hip abnormalities only 19 received any form of treatment 23 of these children were born in the University Hospital and had therefore been examined immediately after birth in the maternity department In 18 out of these 23 cases treatment was considered indicated because of slight ace

Table III Distribution of the children by applied treatment

	Non treated cases	Treated cases			
		Standard treatment	Special treatment		Total treated
			Simple	complicated	
Newborn		( )	6 (1)	1 (3)	21) (?29)
Infants				17 ( )	19

Figur s in paren [illegible] the University Hospital

tabular dysplasia small capital epiphyses or limitation of abduction but no established dislocation As far as we know the hips later developed normally in all these 18 children

The remaining 5 cases (4 typical and 1 atypical) occurred in children with established dislocation who received special treatment

In three of them dislocation of one hip was diagnosed between 3½ and 4 months after birth Closed reduction and immobilization in plaster gave very satisfactory results in all 3 cases In another child dislocation of one hip was diagnosed at the age of 1 year The child had been treated earlier for congenital megacolon but no other congenital abnormalities had been found The dislocated hip was treated by closed reduction and immobilization in plaster also with a satisfactory result

The fifth case (the atypical one) was that of the child with multiple congenital anomalies such as anal atresia urinary tract malformations and deformity of the sacrum Dislocation of one hip was diagnosed soon after birth in about the 4th week of life and was treated first by immobilization in plaster and later because of a pronounced dysplasia of the acetabulum and valgus deformity of the hip by open reduction combined with a varisation osteotomy

Discussion

The present material is composed of a) children born in the maternity department of the University Hospital 295 cases and b) children born in maternity departments of other hospitals in the Uppsala region 78 cases All the children belonging to the first group were examined for abnormalities of the hip joints by a consultant pediatrician as a rule on the first and seldom later than the third day after birth The material of group *a* is therefore considered to be more homogeneous and reliable than that of *group b* and will be analyzed separately below

Altogether 11 868 children were delivered in the University Hospital during the four year period 1962—1965 In 242 newborn the consultant pediatrician found positive or suspected *signs of CDH* by the primary examination These babies were referred to the Orthopaedic Department The *incidence* of referred cases thus amounted to as *much as* approximately 2 % *of* all the births (table IV) Earlier analyses of similar Swedish *materials* have provided data suggesting a lower *incidence* of these abnormalities Thus among 12 391 examined newborn a total incidence of positive Ortolani's click or subluxation *provocation of* 2.7 ‰ has been reported (Palmén 1961) while among 11 375 examined newborn *genuine dislocation* was diagnosed in 2.1 ‰ and doubtful dislocation in another 1.2 ‰ *making* a total of 3.6 ‰ (Emneus 1966)

Among the newborn who received special treatment 7 were born at the University Hospital Five of them had typical CDH and two atypical CDH (myelomeningocele and arthrogryphosis)

In 4 of these latter cases the reason for special treatment was a slight acetabular dysplasia diagnosed at the regular three month checkings After a period of prolonged abduction treatment in plaster the hips of these babies developed satisfactorily

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Table III Distribution of the children by applied treatment

	Non treated cases	Treated cases			
		Standard treatment	Special treatment Simple	Special treatment complicated	Total treated
Newborn	13	232 (222)	[illegible] (1)	4 (3)	2[illegible] (2[illegible])
Infants	[illegible]		32 (18)	1 ([illegible])	1[illegible]

Figures in parentheses denote the number of babies delivered at the University Hospital

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The strikingly higher incidence observed in the present material is undoubtedly attributable to overdiagnosis of these abnormalities in the Uppsala series. The primarily suspected or established diagnosis was verified at the second examination in the Orthopaedic Department in only about 57 % of the admitted, but the incidence is still almost 2 to 3 times as high as that reported earlier. The newborn babies who did not get any form of treatment comprised 5 %, although the primary diagnosis could be verified in only 57 % of the total number of newborn. This means that about 10 % of the newborn underwent the standard treatment in spite of the fact that no signs of hip abnormality could be verified at the orthopaedic examination. The reason for this overtreatment was usually that one or more days elapsed between the two examinations and that the indication for treatment was based on the findings of the primary rather than on those of the second examination.

In 5 cases (including 1 atypical case), or 0.42 % of all the births, an established dislocation diagnosed later was not detected in the maternity department at the primary examination, which thus failed.

The dislocation was detected in all cases but one, however, before 1[illegible] months of age. The primary examiner in the maternity department has a key role, and he is responsible if laxity is overdiagnosed or missed. Repeated examinations in the newborn period seem to be important.

The fact that 3 cases (including 1 atypical), or 0.25 % of the total number of births, showed persistent dislocation in spite of early treatment with a Frejka pillow, indicates that this treatment is not always sufficient. Much better results with the use of the other types of splints have been reported (von

Table IV. Frequency data relating to 11 [illegible] children born between 19[illegible] and 19[illegible] in the maternity Department, University Hospital, Uppsala

	Number	Percentage of referrals	Percentage of total number of births
Newborn referred with suspected CDH	212		2.0
Standard treatment	[illegible]32	[illegible] 8	
Other simple treatment	[illegible]	[illegible]	
Other complicated treatment	8	[illegible]	
Unsuccessful standard treatment in typical CDH	[illegible]	1.[illegible]	
Infants referred with established CDH	[illegible]	–	0.01

Rosen 1956 Palmen 1961 Emneus 1966) The absence of femoral head necrosis or other complications in the children treated with a Frejka pillow however contrasts with the high frequency of complications in children treated with other types of splints as reported at this meeting (Fellander et al 1970)

References

EMNEUS H (1966) Acta Orthop Scand 37 311
FELLANDER M et al (1970) Acta Orthop Scand Suppl 130
PALMÉN K (1961) Acta Paediatrica Vol 50 Suppl 129
VON ROSEN S (1956) Acta Orthop Scand 26 136

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In [illegible] cases (including 1 atypical case) or 0 42 % of all the births an established dislocation diagnosed later was not detected in the maternity department at the primary examination which thus failed

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	Number	Percentage of referrals	Percentage of total number of birth
Newborn referred with suspected CDH	21[illegible]		[illegible]
Standard treatment	232	[illegible]	
Other simple treatment	22	[illegible]	
Other complicated treatment	8	[illegible]	
Unsuccessful standard treatment in typical CDH	3	1 [illegible]	
Infants referred with established CDH	[illegible]	—	0 04[illegible]

Instability of the hip in new born infants
1958 1960
81 children 114 hips

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Fi 1 Distril ution by a e sex an l sit

l p lj lu po ce est appl juee sur la fac interne de la cui se l in lex sur la face anté ri ure l n diu t eten lu le long d sa fac xterne et sa pulpe appuie sur la region troch nt ri nn l annula re t l petit d i t r pliés ntourent l mollet La cui se est maint nu fle h l ngle lroit ur le ba in la jambe est égal ment fléch e a l an le lroit ur la cuis L operat u util se vol nti rs l un de membres inférieurs pour immobili er l l a i j n l nt qu il exam ne l autre Dans un premi r temps la cuis e fixée comme il t lit l p rt er a l l i ti n pen lant q ie h pulp du pouce propulse legèrement de d l n d l or l xtremite d cett uis e et pendant que la commissure du pouce appu ur l g n u Si l l arcl e st subluxabl on sent parfois un secousse due a la s bl xati n l la têt femorale Dans un d uxième t mps l operateur imprime a la u n d placen nt nv rse La pulpe du médius pou se le trochanter d arriere en avant t l d l n l l n p ndant qu la cuis e est p rtée en abduction Par cette manœuvre il st i l luxe la têt rentre dans la cavite cotyloïde par de sus le bord postérieur et e ti r tré a compagn toujours d un re saut l arfois lég r souvent forte net il arrive l r saut o t assez bruyant pour qu on l entende

The *clinical examination* in our cases was made

partly as simple abduction or adduction without exerting any pressure at all on the thigh in any direction

partly by using the technique described by Le Damany for provocation of the ressaut

We observed three degrees of instability which were not sharply *defined* and the following clinical grouping was obtained

Instability of the hip in the newborn

Classification for selective treatment, pathogenesis of the dislocation and complications

BY M. FELLANDER, H. GLADNIKOFF & F. JACOBSSON

Since 1958 examination of the hips in newborn infants by Ortolani's method has been a routine procedure in the maternity units in the Stockholm area. Ortolani's "segno dello scatto" ("signe de ressaut") signifies *essentially that there is a ridge over which the femoral head is felt to glide. "A click" is an unfortunate error in translation of segno dello scatto.* Clicks of unknown nature can often be felt on palpation at Ortolani's manoeuvre but, unlike gliding, they are harmless phenomena which have no relation to Ortolani's sign. We prefer the term "ridge phenomenon".

Own material

In the Stockholm area virtually all the infants with suspected hip dislocation have been transferred to the *Children's Hospital Samariten for* further investigation and treatment. Over the period 1958–1960 we found 114 hips with gliding over a ridge in 81 newborn examined clinically and radiographically at 1 to 4 days of age. The distribution by sex and involved side will be seen in Fig. 1. They were followed clinically and radiographically up to the age of 5 to 7 years with the exception of 11 children who were observed only up to the age of 2 to 4 years and could not be traced for follow up examination.

Clinical examination

Clinical examination is in the main carried out in the same way as that originally described by Le Damany and commendably revived by Ortolani (and by Palmen in Sweden). In its classical simplicity Le Damany's description of this "ressaut" deserves to be quoted here:

L'*enfant* est couché sur le dos sur une table. L'opérat[illegible]ur [illegible] placé en face [illegible] lui. Avec douceur, sans aucune force, il saisit chacune des jambes du n[illegible] avec la main d[illegible] opposé de telle sorte que la commissure de son p[illegible] [illegible] le genou de l'enfant

From the Children's Hospital Samariten and the Orthopaedic Department, St. Göran Hospital, Stockholm.

Instability of the hip in new born infants 1958 1960

81 children 114 hips

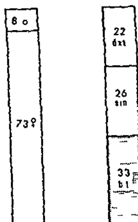


Fig 1 Distribution by age sex and site

La pulpe du pouce est appliqué sur la face interne de la cuisse, l'index sur la face anterieur, le medius est étendu le long de sa face externe et sa pulpe appuie sur la région trochantérienne, l'annulaire et le petit doigt repliés entourent le mollet. La cuisse est maintenue fléchie à l'angle droit sur le bassin, la jambe est également fléchie à l'angle droit sur la cuisse. L'operateur utilise volontiers l'un de membres inférieurs pour immobiliser le bassin pendant qu'il examine l'autre. Dans un premier temps la cuisse fixée comme il est dit est portée en adduction pendant que la pulpe du pouce propulse legérement de dedans en dehors l'extrémité de cette cuisse et pendant que la *commissure du pouce* appuie sur le genou. Si la hanche est subluxable on sent parfois une secousse due à la luxation de la tête fémorale. Dans un deuxième temps l'opérateur imprime à la cuisse un déplacement inverse. La pulpe du médius pousse le trochanter d'arrière en avant et de dehors en dedans pendant que la cuisse est portée en abduction. Par cette *manœuvre* si elle est possible, la tête rentre dans la cavité cotyloïde par *dessus le bord postérieur* et cette rentrée s'accompagne toujours d'un ressaut. Parfois le ressaut souvent fort net, il arrive que ce ressaut soit assez bruyant pour qu'on l'entende.

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From the Children's Hospital Samariten and the Orthopaedic Department, St. Göran Hospital, Stockholm

and ischium are projected in the same transversal plane The thighs should be extended in the hip joints and rotated inwards so that the lesser trochanters are barely visible (Fig 2) The ossification zones of the acetabular roofs will be clearly visible and on subsequent films in the same view even small deviations from the rapid neonatal ossification process will be seen

Anatomy of the hip in the newborn Two thirds of the acetabular roof are chondral (Fig 3) The osseous surface of the roof appears plane and steeply sloping and is very short (Fig 2) The bone usually ends laterally in a margin at the transition into cartilage This margin is very small or absent at late ossification This is not dysplasia but an *ossification anomaly*

A periacetabular recess on the outer side of the edge of the labrum is visible in anatomic specimens (Fig 3) At *arthography* the contrast in this recess (Fig 4 b) indicates the position of the edge The adjoining half of the acetabular roof is still chondral The *articular surface* of the roof consists of a single caudally directed concavity Consequently the plane steeply sloping short osseous surface of the roof *is unusable in the assessment of the articular surface* The pressure from the femoral head is distributed over the entire acetabulum

The *morbid anatomy* is visible in arthrograms (Figs 4 a 5 6 and 7) The medial part of the acetabulum is empty before the femoral head is felt to pass over the ridge (Fig 4 a) which means that it is not in contact with the joint head The pressure from the femoral head is still concentrated wholly on the lateral part of the roof which is still chondral and has kinked it cranially As a result the concavity of the acetabular roof is divided into a medial osseous part and a lateral chondral part An intersection between



Fig 2 Standard X ray of pelvis of a newborn The cranial borders of the pubis and ischium in the same transversal plane The ossification zone of the acetabular roof is clearly visible

1 *Instability without dislocation*—the joint head is in normal and constant position in the acetabulum but can be dislocated dorsally (subluxation provocation)

2 *Instability with inconstant dislocation*

3 *Constant dislocation*

We based the indications for treatment on these degrees of instability

Instability without dislocation disappears within 1 to 7 days (occasionally longer time) treatment is not necessary

Instability with inconstant dislocation implies that a ridge or gliding phenomenon (signe de ressaut) is felt once or several times at repeated examinations Spontaneous correction and stabilisation can also occur within 1 or 2 weeks in these cases All cases will not heal spontaneously however It takes an experienced examiner to decide whether to treat such a hip promptly or to await possible spontaneous regression We have sometimes used expectant treatment for up to 2 weeks before making the final decision In each case this decision was then based on the X-ray examination together with the tendency to spontaneous healing

Constant dislocation is treated promptly by immobilisation in an abduction splint

The group that was thus left untreated but was under careful observation comprised 39 children with 45 affected hips (Table I) The remaining 42 children with 69 affected hips were treated in a von Rosen splint for 2 to 4 months Most of them were kept in the hospital for a short time so that the mothers could learn to nurse them in their splints The splints were removed at bathing or changing of nappies care being taken to assure that the child s legs remained in the abducted position

X ray examination

The initial X ray examination of the newborn requires only one straight anteroposterior view of the pelvis in which the cranial borders of the pubis

Table I Instability of the hip in newborn [illegible]

Examination technique	Treatment	No of children	No of hips
Ortolani s abduction manoeuvre	Abduction splint 2 4 months	42	69
Subluxation provocation	*None*	39	45
Total		81	114



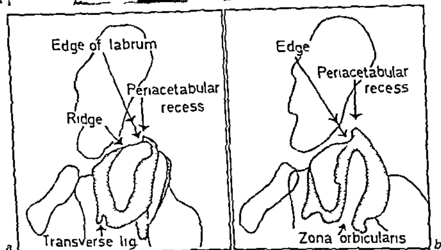


Fig. 4 Th rid e phenomenon

a) The d located hea I h s no contact with th med al part of the acetab ilum Its pressure k nk th chondral part f th r of cran ally and as a result the roof is divided into a m dial an I a lat ral conca its The intersecti n between the two concavities forms a ri ( ) Th periac tabular r ce s ( ) ind cates the d e ( ) of the labrum

b) Aft r r duction th a tabulum is one concavity up to the e ge of the labrum ( ) It r u i di t ibut d over the ntire acetabulum The kink an I the ri ge are lim nat d

with the head outside the acetabulum and with the labrum infolded by the dislocated head could not be demonstrated in any of the cases

Secondary changes may arise at three sites around the line *between the* bony margin in the acetabular roof and the lesser trochanter namely 1) in the osseous margin of the roof 2) in the head and 3) in the neck usually they are combined (Fig 6) The initial appearance of the changes as well

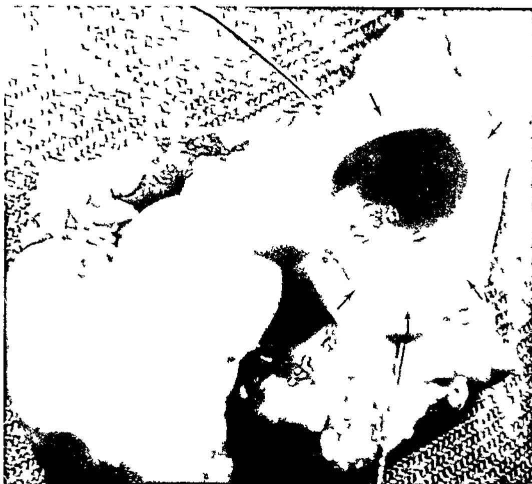


Fig 3 Specimen of hip in a newborn Only the dark area in the centre of the acetabulum is ossified about one third of its surface The light periphery is entirely chondral and comprises two thirds of its surface The joint capsule is attached to the outer side of the acetabulum 2—3 mm from the rim with resulting formation of a periacetabular recess all round the outer side (the recess is indicated by arrows)

the two concavities must form a ridge this *ridge is visible where the femoral head loses its contact with the acetabulum*

Abduction brings about a reduction The kink the lateral concavity and the ridge are eliminated at the reduction They reappear after the corresponding dislocation manoeuvre Consequently the ridge visualised by arthrography in our children corresponds to the ridge that can be felt during the performance of Ortolani s abduction manoeuvre These reversible changes cannot be expected always to remain visible when the joint is opened and the head removed for inspection of the roof because the pressure of the head is then eliminated

Both cranial kinking of the acetabular roof and the ridge phenomenon were present in all the 9 children who were examined at an early stage by arthrography In 2 of them the ridge bilaterally was more distinct (Fig 5) the two concavities here intersect each other at almost right angles Luxation

Such changes in the femoral head were noted in 43 hips of 28 children (Table II) Over bridging of the ossification defects in the head begins at about 1 year of age The bony structure and the shape become slowly normal up to the age of 5 to 8 years Flattening of the head and incongruence with the acetabulum may persist however especially if bone changes have also been present in the neck

Changes in the neck of the femur are often visible initially as small ossification defects shaped like an axe cut or as a step like progressive break (Fig 6) in the bone close to the epiphyseal cartilage and may appear before or after the ossification of the head When the ossification of the head begins the axe cut in the neck often proves to be a continuation distal to the epiphyseal cartilage of a lamellar ossification defect through the head and like this it is frontal or sagittal

The axe cut or break may grow deeper and wider to become cup shaped this weakens the neck and may result in ante or retroversion of the head and in varus deformity of the neck (Fig 7 g) Bulbiform rarefaction hyper mineralised clumps as well as bone absorption are often present as in the head

Femoral neck changes occurred in 32 hips of 21 children and were in every case associated with lesions of the head

The bone changes in the neck disappear partially or entirely before the age of 5 to 8 years except for any varus deformity which may persist

Distinct but slight femoral head changes developed in 4 hips of 4 out of the 39 children who were left untreated because the instability was not attended with constant dislocation and became quickly corrected In these 4 hips the bone changes disappeared completely Dislocation with abnormal pressure could have been present prenatally and caused the changes Too ungentle or repeated examinations are another possible cause that cannot be excluded

Bone changes also developed in 4 hips without demonstrable instability in 14 children with instability of one hip for which they were treated by immobilisation in a position of abduction These bone changes disappeared only partly but in no case did they cause any apparent functional disturbance apart from some limitation of abduction

Follow up examinations and results

70 of the 81 children were re-examined at the age of 5 to 7 years As regards the other 11 the results were assessed from the last examination at the age of 2 to 4 years Clinical and radiographic results will be reported separately in the following

as their connection with the dynamics of the dislocation and with one another are of interest

Ossification defects in the acetabular roof are seldom visible as early as the first days of life (Fig 6 a) they usually develop at the age of 1 to 3 months in bone tissue that is normal at birth (Fig 7) They may appear shallow or cup shaped or more well marked at the site of the bony margin of the roof and are often associated with retardation of the normal decrease in the inclination of the bony roof during the neonatal period This dysplasia hypoplasia or false acetabula gradually increases or remains until reduction takes place

Such ossification defects in the acetabular roof were found in 33 hips of 24 children (Table II) In 4 children such defects also developed on the side on which no gliding over a ridge was noted The defects in the healthy hips were probably residual changes after dislocation which had healed after spontaneous reduction and stabilisation of the joint prenatally

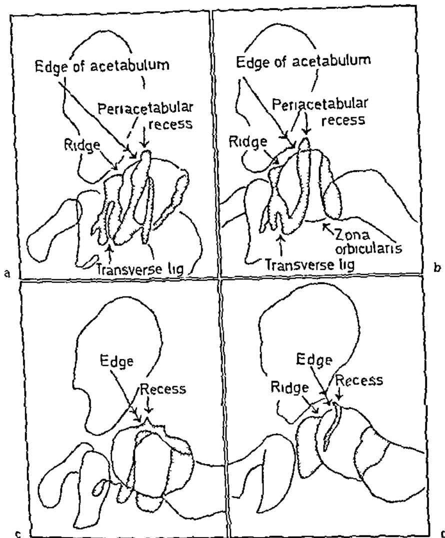
Changes in the head of the femur are more common than in the acetabulum and in the neck The ossification of the head is retarded and proceeds slowly The bone nucleus may be wholly (Fig 7) or partially (Fig 6) divided into two parts by a frontal or sagittal ossification defect either shaped like the cut of an axe or lamellar Marginal ossification defects giving the bone nucleus an irregular shape are often present as well The bone structure primarily or secondarily shows bulbiform rarefactions and hypermineralised clumps The head as well as its bone nucleus often become flattened

Table II Secondary bone changes in 81 children with 114 dislocated hips

Localisation	No of children	No of hips
Acetabular roof	24	33
Head	28	43
Neck	21	32

Table III Secondary bone changes

Localisation	No of hips	
	During the course	At after examination
Acetabular roof	33	8
Head neck	43	10



Fı A 1 week old child with in tab il ty of the hip
) Ext n ion The di located l ea l kinks th chondral part of the acetabulum cranially with r ulting formation of a ri l ((↘) at the site of kinkin The periacetul ular r r ( ) mark the cartila inous circumfer nce of the acetabulum from the cr nial n) (↘) to the transverse li ament ( ) The cranial labrum is not infolded but m l a l kink d cranially
( ) 4 al 1 ict on D slocation Th cranial kinking of the labrum (↘) and the ridge (↘) ar l ss rke l
c) 90 bdu tion Reducti n The pressure of the head is distributed over the entire acet lulum Tl e rid e an l th cranial kinking of the labrum (↘) are elim nated
) 90 bduction Repe t l n ore marke l dislocation provoked by light pressure from b) d on th proximal part of the femur Th cranial kinking of the labrum is visible an l i more marke l than before

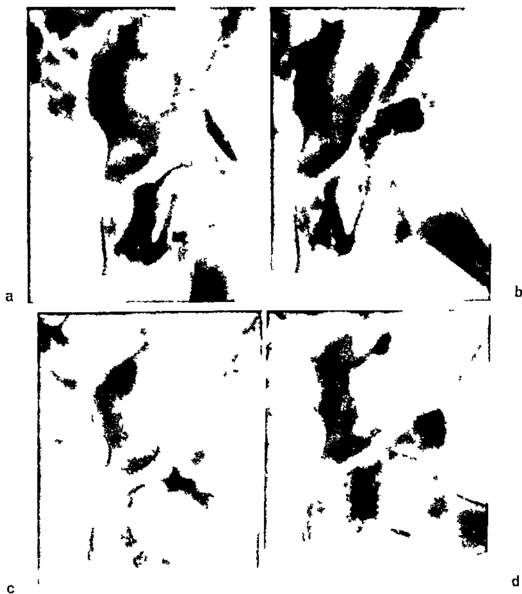
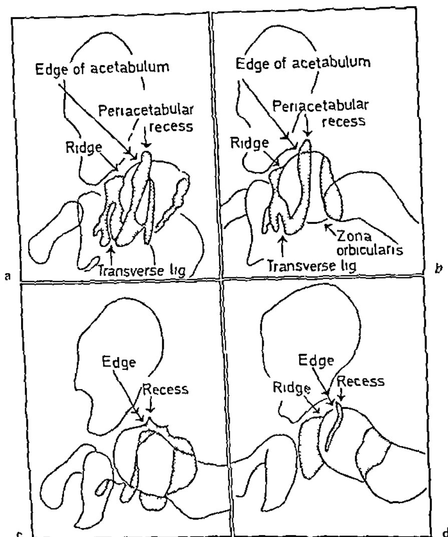


Fig. 5



(A 1 week old child with instability of the hip
) F t n i n Th h locat l head kinks th chondral part of the acetabulum cranially with resulting formation of a ridge (↓) at the *site of kinking* The periacetabular rec ( ) marks the cartilaginous circumference of the acetabulum from the cranial rim (↓) to the transverse ligament ( ) The cranial labrum is not infolded but in te l kinked cranially
b) 4 abduction D location The cranial kinking of the labrum (↓) and the ridge (↓) ar marked
) 30 abduction R duction The pressure of the head is distributed over the entire acetabulum The ridge and the cranial kinking of the labrum (↓) are eliminated
d) 30 abduction Repeated more marked *dislocation* provoked by light pressure from behind on the proximal part of the femur The cranial kinking of the labrum is visible and is more marked than before



Fig. [illegible]

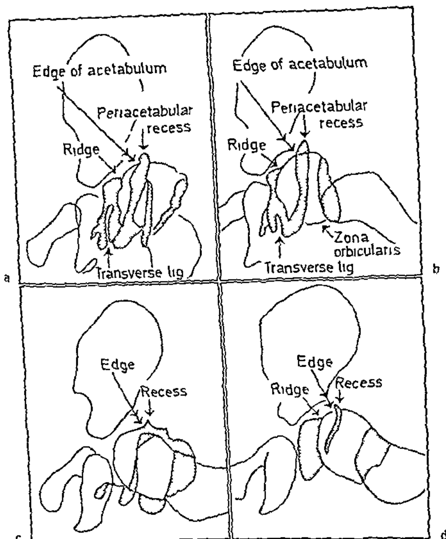


Fig [illegible] instability of the hip
[illegible] The [illegible] kinks the chondral part of the acetabulum cranially with [illegible] formation [illegible] a ridge (↓) at the site of kinking. The periacetabular [illegible] marks the [illegible] circumference of the acetabulum from the cranial [illegible] (↓) to the [illegible] ( ) The cranial labrum is not infolded but in [illegible] cranially
[illegible] Dislocation The cranial kinking of the labrum (↓) and the ridge (↓) are [illegible] marked
[illegible] Reduction The pressure of the head is distributed over the entire [illegible] The ridge and the cranial kinking of the labrum (↓) are eliminated
[illegible] more marked dislocation provoked by light pressure from [illegible] on the proximal part of the femur The cranial kinking of the labrum is visible and [illegible] than before

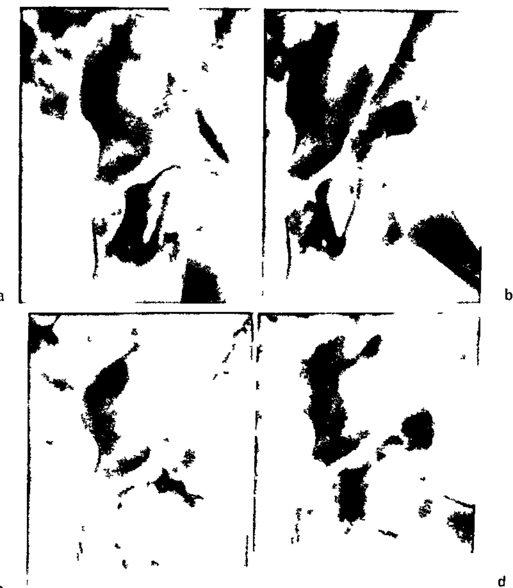


Fig. 3

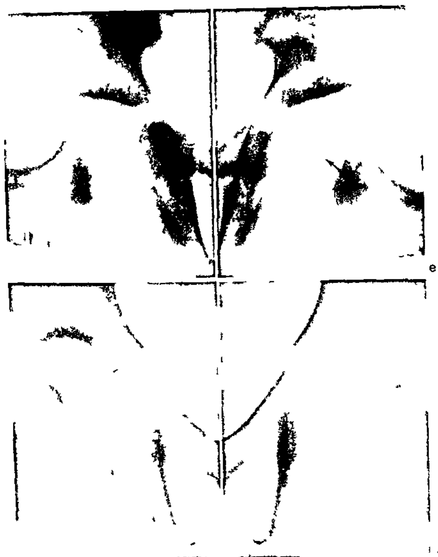
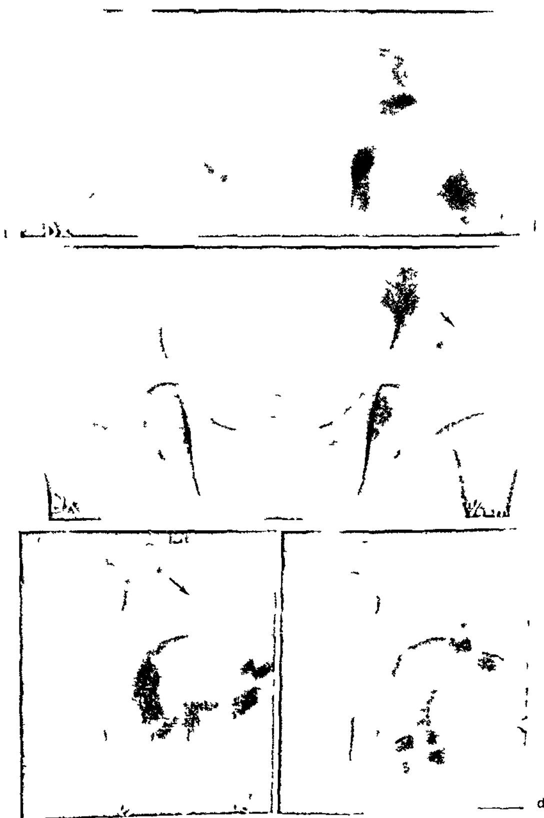


Fig C Slight secondary bone changes in the roof and head
a) 5 days No bone change in the acetabular roofs
b) 5 months Ossification defect in the left labrum (↘) The bony surface of the right acetabular roof is normal the inclination of the bony roof on the left side has not decreased normally because of retarded ossification
c) 6 months Extension The joint head is dislocated It pressure is concentrated on the chondral part of the acetabulum kinks it cranially and is transmitted to the ossification defect (↘)
d) 6 months 90 abduction Reduction causes the pressure to shift to the caudal part of the acetabulum thus relieving the roof and the ossification defect The kinking is eliminated
e) 2 years An axe cut shaped frontal ossification defect (↖) is visible subchondrally in the left joint head The vacuum phenomenon shows that the cartilage is normal over the bone defect
f) 4 years Only suggested dysplasia of the left acetabular roof and slight structural change and flattening of the joint head


d



1 ig I ronounc l l on chan c in th roof head and neck
a) 1 da Mın mal o sification d f cts (↓ and ↘) in the acetabular roofs
b) w k Th o ıfication d f ct hav increased ın size and the inclination of the bony r f h n t l er asc l
c) w k l xt nsı n Th l sl cated joint I ead presses the lateral part of the acetabular ro f cran lly Tl pr sure ı transmitted to the bone defect (↓)
d) w ks 10 ab l ction Al reductı n the pr ssure of the head on the roof and the bone d f ct ı (ıı)ınat f
) 7 n onths (Afl r treatn nt in an abduction splint for 2 months) Only small remnants of th l ne j f ct Th inclination of the bony roofs has become *normal* A *frontal* 11 h pe l sf cat on d fect ıs seen ın th right joint head (↓) *extending in the* shape f an ax ut into the neck cl se to the epiphyseal cartilage (↑) *The* ventral bor l r of th f m ral n ck is presse l di tally (↖)
f) 12 month l rogre s
g and h) t ars l ersı ting dy plasia of the *left* acetabulum and deformity of the left j int h a l with fragmentation of the bone *nucleus* *Slight* changes ın shape and ☛ cture of the right head and neck Varus deformity bilaterally

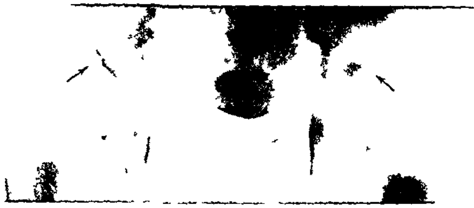






Fig. 7 Pronounced bone changes in the roof head and neck
a) 1 day Minimal ossification defects (↙ and ↘) in the acetabular roofs
b) 7 weeks The ossification defects have increased in size and the inclination of the bony roofs has not decreased
c) weeks Extension The dislocated joint head presses the lateral part of the acetabular roof cranially The pressure is transmitted to the bone defect (↙)
d) weeks 90 abduction At reduction the pressure of the head on the roof and the bone defect is eliminated
e) months (After treatment in an abduction splint for 2 months) Only small remnants of the bone defects The inclination of the bony roofs has become normal A frontal slit shaped ossification defect is seen in the right joint head (↙) extending in the shape of an axe-cut into the neck close to the epiphyseal cartilage (↗) The ventral border of the femoral neck is pressed distally (↖)
f) 12 months Progress
g and h) 4 years Persisting dysplasia of the left acetabulum and deformity of the left joint head with fragmentation of the bone nucleus Slight changes in shape and structure of the right head and neck Varus deformity bilaterally

Clinical results In 1 child with a bilateral ridge phenomenon dislocation of one hip could not be reduced either by splintage or by other closed orthopaedic measures Open reduction was performed at the age of 1 ½ years As regards the other 113 hips reduction was achieved by treatment in a splint and resulted in permanent stability At the follow-up examination all the children were subjectively free from symptoms Objectively Trendelenburg s test was negative and walking ability normal in all the cases but a *slight limitation of abduction was noted in 10 cases*

Radiographic results An ossification defect in the *acetabular roof* was still present at the follow up examination in 8 hips of 6 children (Table III) In one of them who had dislocation of one hip joint extensive changes were also present in the femoral head and neck with varus deformity In the remaining 7 hips the examination showed only slight dysplasia of the acetabular roof without any other radiographic abnormalities

Changes in the *femoral head* possible also in the *neck* were noted in 40 hips (Table III) They were designated as slight in 19 moderate in 8 and severe in *13 hips The latter group was characterised by marked deformity* of both the head and the neck Varus deformity of varying degree was noted in 11 hips of 9 children in 2 of them so severe that corrective osteotomy was performed

Discussion

With respect to *treatment* our series of cases differs from other series reported at this symposium in that we left some clear-cut cases untreated *This policy had no ill effects in the form of persistent dislocation or* dysplasia of the acetabulum

Many workers use immobilisation in the abducted position for every unstable hip irrespectively of the character of the instability as immobilisation in the abducted position will not do any harm Long term immobilisation however can be followed by more or less marked bone changes in the head and neck of the femur possibly as a result of nutritional disturbances in an abnormally fixed position

As regards the X *ray diagnosis* Caffey 1950 states Roentgen diagnosis during the neonatal period and first months of life is exceedingly difficult and often congenital dislocation can be neither identified nor excluded satisfactorily on the basis of roentgen findings Andren and von Rosen in 1958 published a new projection with inward rotation and 45° abduction of the legs It was claimed to demonstrate hip dislocation with certainty in the new*born* a line through the long axis of the femoral shaft should pass through or cranially to the lateral edge of the roof But as will be seen from Figs 4 and 8 this new projection can be misleading and like the old one it

c d e

[illegible] 8 Limitation of X-ray diagnosis

a) [illegible] dislocation [illegible] present [illegible] the extension of the [illegible] of the acetabular roof when the [illegible] inward rotation at [illegible] abduction

b) [illegible] later however for instance because the head can be [illegible] easily [illegible] spontaneously or by slight changes in inward rotation or abduction

c) Dislocation

d) [illegible] abduction

e) Dislocation [illegible] provoked by slight pressure backwards—cranially

can often neither identify nor exclude dislocation It can be misleading because 1) the joint head can be temporarily reduced at this projection 2) the projection will not always be exact and 3) the position of the *bony margin of the acetabular roof* varies at varying degree of ossification and *is not identical with the acetabular margin* The latter is chondral neonatally and situated about 1 cm lateral to the bony margin

In the early part of our work with neonatal hips we used arthrography as a means of studying the pathological anatomy and in particular the nature of the ridge in the hope of obtaining further insight into the nature of the disease and guidance in the treatment But arthography is too complicated as a routine method and not entirely free from risks X ray examination 1 ½ to 3 months later, on the other hand, will show any deviations from the normal ossification of the acetabular roofs that is the condition can be assessed at a time when the clinical findings including the ridge phenomenon are not certain A comparison with films of the hips during the neonatal period will make the assessment easier

Our arthrographies have shown that the ridge phenomenon is due to cranial kinking of the labrum with resulting formation of a ridge A well marked ridge of this type (Fig 5) observed in 2 cases was earlier interpreted by orthopaedic surgeons and radiologists (Severin Caffey, and others) is a labrum that is infolded by a luxated femoral head The following two details indicate that this is not the case 1) The periacetabular recess demonstrates the edge of the labrum at a point about 1 cm craniolateral from the ridge hence the edge is not infolded 2) A 15-degree abduction of the femur shifts the pressure of the femoral head medially towards the ridge which will then assume the same flat shape and size as in the other 7 arthrography cases (Fig 5) The cartilagenous part of the acetabular roof in these 2 children seems to be unusually soft the well marked ridge is otherwise of the same kind as the flat ridge in the others *Accordingly in all hips of 9 newborn infants examined by arthrography the dislocation was a subluxation caused by insufficient firmness of the chondral part of the roof* This insufficiency explains the instability of the head in the acetabulum

Reports on newborn infants with the head of the femur wholly outside the acetabulum as in older children with inveterate dislocation have been published by other investigators but their cases would appear to be exceptions or to have been incorrectly interpreted

Secondary changes The *changes in the roof* should not be mistaken for the *normal variation* already mentioned and seen in *late ossification* namely bilateral absence of ossification of the acetabular roof or very small osseous margins with unusually steep but symmetric inclination of the bony roof The remaining ossified part of the acetabulum appears extremely shallow This is not dysplasia as Putti believed for the bony margin appears a few

weeks later and the acetabulum including its chondral roof has normal shape and depth increases and the inclination decreases as ossification proceeds The chondral acetabular roof is usually normal in firmness and function

The defects may be produced by the pressure from the dislocated femoral head The entire pressure is concentrated to the cranially kinked chondral part of the roof (Figs 5 6 and 7) and in this pre osseous cartilage the ossification ceases If unilateral the damage results in asymmetry of the hips The defect demonstrates that there is or has been a dislocation

Our pressure damage theory is supported by the fact that reduction which eliminates this abnormal pressure is followed by normalisation This begins with ossification from the bottom of the defect and at the same time the inclination of the bony roof decreases its length increases and it becomes normal or subnormal with slightly concave surface The normalisation of the roof is usually completed when the ossification of the head begins As a rule normal conditions of the roof are completely re instated within the first year of life but in 8 hips the bony roof remained tilted cranially and became rough and sclerotic It may then be difficult or impossible radiologically and without arthrography to determine at once whether this residual change is due to failure of reduction or merely to slow normalisation

Changes in the head and neck of the femur are much more common in our cases than in other published series One —and the main—explanation of this would probably be that more or less uncertain cases with inconstant clicks etc were not included in our series which meant a more concentrated and selected primary material Another reason could of course be that very slight radiographic late changes were also recorded in our cases The fact remains however that the changes were pronounced in 11 % of the total number of cases and varus deformity was so severe in 2 cases that corrective osteotomy had to be performed The possibility cannot be excluded that too rigid immobilisation in the splint could (via nutritional disturbances) have given rise to these changes in the head and neck of the femur

Summary

The series comprises 111 hips in 81 newborn infants with Ortolani s ridge phenomenon from the period 1958 – 1960

The nature of the ridge phenomenon was demonstrated by arthrography The pressure from the joint head kinks the chondral part of the acetabular roof cranially with the result that a ridge is formed at the transition into the osseous part of the roof

Bone changes in the acetabular roof were present in 33 hips and were still noted at the follow up examination in 7 % of the cases

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Brief contributions to the subject

NILS LINDSTRÖM, HÄRNÖSAND

My contribution to the discussion on the unstable hips will be a short account of our experiences in the Orthopaedic Clinic at Härnösand. Owing to the situation of our clinic at a fair distance from each of the county's general hospitals we were rather late in starting to receive fresh cases. Between 1958 and 1959 only 1 fresh case in a newborn infant was referred to us and in each of the years 1960 and 1962 we received 2 cases. During the same period of time the following numbers of "missed" cases were treated in the clinic: 12 cases in 1958, 5 cases in 1959, 2 cases in 1960 and 1 case in 1961. This means that in the first period 1958 to 1961 we treated only 6 newborn infants with unstable hips while at the same time we had 20 "missed" cases. I have now looked through the records from this period and found that the latter group included babies who had earlier been treated on a frame which had been removed at bathing or changing of nappies. In consultation with the paediatricians in the county it was agreed upon that from then on we should primarily have the care of all infants with suspected hip dislocation.

In the following five year period we received and treated 15 newborn babies in 1962, 10 in 1963, 22 in 1965, 33 in 1964 and 16 in 1966, all being cases of unstable hips. But each year we still received, on an average, 1 case which had been missed at birth. So over the period 1962—1966 we treated 96 infants with unstable hips who were referred to us before they were one week old or, in some cases, at the age of eight days. Over the same period of time we received 6 "missed" cases. It is probably to be expected that a few cases will always be missed at the routine examination after birth, all the more so as all the hospitals in the county except two lack paediatric service.

We have placed every newborn infant with an unstable hip in a von Rosen splint, which was not removed at changing of nappies or at bathing. The splint was left on for three months. I have not been able to find any case of redislocation among the 102 "fresh" cases thus treated over the period covered by the study, 1958—1966.

But on looking through the records I noted a detail that seemed worth

Ossification defects of the head and neck of the femur were present in 13 hips and at follow-up examination found to persist to a marked degree in 11 % of the total number of cases

Clinical manifestations of these bone changes are usually absent but 2 of our patients had varus deformity of such a degree that corrective osteotomy was necessary

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Fi 1 Girl born 1(/o 196 Reeuction under anaesthesia 1(J 196 Immobilize l in plaster for 3 months X ray pic tur al ove at the age of 1½ year



Fig 2 The same girl as f g 1 at the a e of 2½ years Note the ostcochon lro is

Osteochondrosis of capitular epiphysis has been up for discussion The Lund series from 1961–1961 included no cases that could be so designated But I can show *one case* from the Orthopaedic Department at Uddevalla

Case report A girl born in May 196 dislocation was not detected until she was three months old She was then examined under anaesthesia and immobilized in plaster for three months When she was six months old the nucleus of the dislocated hip was very small A change in the epiphysis can be seen but at this stage the appearance does not resemble that of osteochondrosis At the age of 1—2 years there is distinct fragmentation of the epiphyseal nucleus See figs 1 and 2 This is of course a case of late treatment of more classical type and not of treatment in the newborn period

reconsidering I discovered that there were several infants who had not been brought back to us for routine checkings after the splint had been removed at the age of three months Some infants may of course have died or been taken elsewhere for re-examination Although none has been referred to us again with redislocation it is not satisfactory, as we should have liked to follow them up to the age of three years

Therefore I have in mind to start a card index system like that used in *the tumour centre at the Radiumhemmet* so that children who do not return as arranged can be called to appear for re examination I should like to know your experiences and your opinion as regards this detail of the follow-up of newborn babies with unstable hips

HANS EMNEUS UDDEVALLA

I have not had time for a complete re-examination of the records of my old Lund series *dating back to the period 1961—1964 I have* been able to confirm however that one case was missed in the Maternity Department at Lund in 1964 The case was diagnosed as typical classical dislocation in the autumn of 1965 in the Orthopaedic Clinic at Lund No other cases were missed *over the period 1961—1964*

As was mentioned in my paper of 1966 some of the children had by then been observed for just under one year During the past year however there have been no developments suggesting that the infants born in 1964 would show complications other than those seen in the years 1961—1963 But as I have no new actual figures I will make some comments in quite general *terms*

In the introductory papers read today the most important statement was that made by Andren referring to the instability of the hip in the first week of life This is where the age-limit should be set If the affected joint is treated and reduced within the first week of life the course will be very favourable Immobilization in the first week of life is of greatest importance Towards the age of two or three weeks the clinical diagnosis will be difficult and this is where radiographs will play a part After the age of three weeks examination under anaesthesia will often be necessary The joint must then be dislocated so as to verify the abnormality The answer to Weismann's extremely pessimistic report from Israel about their failure of treatment in a von Rosen splint is very likely that the babies were not examined in their first week of life or that the splint was not applied properly In fact the reduction was *not made* immediately

General discussion

COMPILED BY MAC FELLANDER STOCKHOLM

The main questions discussed at the symposium were

1 Clinical diagnosis and incidence
2 Treatment
3 X ray examination
4 Secondary bone changes
5 Missed cases

1 Clinical diagnosis

JACOBSSON pointed out that Severin in his series published in 1941 reported an incidence of only 0 9 per mill This figure would be representative of the incidence in Sweden The Stockholm series at present amounting to 600—700 infants comprises about 2 per mill of the number of births In the Uppsala series presented here the incidence was 20 per mill It cannot be possible that Ortolani s sign was present in 20 per mill of the cases This must be a matter of over diagnosis Surely the figure includes insignificant clicks which have nothing to do with Ortolani s sign The incidence must be of reasonable proportions The criteria for the diagnosis should be stricter so that the materials can be compared

This would also hold true for the assessment of the prognosis as regards secondary bone changes In the Stockholm area the paediatricians have now learnt to recognize Ortolani s sign and most of the babies referred for treatment have shown the ridge phenomenon This may account for the higher incidence of secondary bone changes in this series

SEVASTIKOGLOU stated that the incidence of 20 per mill reported in the Uppsala series relates not only to babies with Ortolani s sign but to all the babies referred to the Orthopaedic Department Cases of suspected laxity or a positive provocation manoeuvre by Palmen s technique are also included

HIRSCH agreed with Jacobsson that the paediatricians who carry out the systematic examination of hips in the newborn must be taught the way to demonstrate abnormal movement of the hip joint When we achieve greater

It has been asserted that early treatment that is starting on the first or second day of life would prevent the development of the late changes in the *head and neck of the femur with which we are concerned here To verify this* I have in co operation with Alvin paediatrician at the Sodersjukhuset during a period of just over one year treated every infant with a proven Ortolani s sign in a splint from its first or second day of life When the mother left the maternity ward the baby was transferred to me for continued checkings and follow-ups This means that there was no elimination of cases of spon taneously healing hip with Ortolani s sign as there had been in the reported material at this symposium The other day I looked through the records of Alvin s and my series which by now is 1½ to 2 years old and found that the said X-ray changes were present in 13 out of the 46 infants or in nearly one-third of the cases In assessing this figure it should be remembered that during this period Alvin placed every child with clicking hips in a splint and so some babies were treated who according to the principles applied by me would have needed no treatment but merely observation

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It has been asserted that early treatment that is starting on the first or second day of life would prevent the development of the late changes in the head and neck of the femur with which we are concerned here To verify this I have in co operation with Alvin paediatrician at the Sodersjukhuset during a period of just over one year treated every infant with a proven Ortolani s sign in a splint from its first or second day of life When the mother left the maternity ward the baby was transferred to me for continued checkings and follow ups This means that there was no elimination of cases of spontaneously healing hip with Ortolani s sign as there had been in the reported material at this symposium The other day I looked through the records of Alvin s and my series which by now is 1½ to 2 years old and found that the said X ray changes were present in 13 out of the 46 infants or in nearly one third of the cases In assessing this figure it should be remembered that during this period Alvin placed every child with clicking hips in a splint and so some babies were treated who according to the principles applied by me would have needed no treatment but merely observation

3 X-ray examination

Hult did not believe that much was gained by X-ray primarily. Of course it is all right when the examination is carried out by an experienced radiologist like Andrén in Malmö but such expert radiological service is not available to every orthopaedic surgeon. There is also the risk that we will get the wrong information by the X-ray examination and further the idea might gain ground among paediatricians and orthopaedists that the disorder should be diagnosed by X-ray. If it could be proved to have any advantages X-ray at birth should of course be used.

Andrén replied that unless it can be properly performed X-ray examination should of course be omitted. The radiologist must be interested in this abnormality. Most radiologists are not—they simply take a picture. He agreed with Hult that we are likely to miss cases if we rely on the radiograph.

Hirsch hoped that the interest in X-ray examination of these children would by now have been stimulated and that the radiologists would acquire the particular technique.

Hult considered that this type of X-ray examination differed from others in that the radiologists must be able to establish a clinical diagnosis which they should then verify by X-ray.

Andrén had had one case in which the paediatrician had suspected hip instability but in which he was not able to feel any slipping movement clinically, whereas X-ray showed genuine dislocation.

[illegible] with experience from Lund and Uddevalla, where patients are referred from large regional hospitals, has managed without primary X-ray examination.

Lindström raised the question whether the repeated dislocation provoked at X-ray examination might injure the epiphyseal nucleus. He *emphasized* that the infants are subjected to so many examinations, first by the paediatrician, then by the orthopaedist and finally by the radiologist.

Jacobsson did not think that X-ray was necessary primarily if there is clear clinical evidence of a true Ortolani's phenomenon. But up to now their policy has been to examine every infant by X-ray at the first visit. In some cases dislocation was diagnosed clinically when X-ray was negative. These infants were of course treated. Jacobsson believes, however, that checking by X-ray is necessary later on; in his cases it is usually made when the children begin to walk. This would apply to uncomplicated cases, but as soon as there is some doubt or when there is limitation of *abduction* films are taken earlier. The present routine is to use *radiographs* at the age of 12—15 months and then at the age of 3 years and 6 years. This has meant a fairly great reduction of the X-ray *dose*.

uniformity with respect to the diagnosis the calculations of the incidence will be more consistent throughout the country It is not possible that the incidence can vary so much as today s reports would suggest One could accept a wider field of indications if one knew for certain that the treatment would not cause any damage

2 Treatment

The subject of discussion was how and for how long the babies should be immobilized According to reports at the symposium a Frejka pillow was used in Gothenburg and Uppsala and von Rosen s splint in the other orthopaedic departments

Hirsch who had experience with the Frejka pillow brought up the question whether this method might involve the risk of dislocation being caused during the course of treatment On the other hand he asked if the rigid immobilization in a von Rosen splint could give rise to disturbances in the growth of the bone nuclei

von Rosen emphasized that it was important to ensure that the joint head be kept in place for the first few weeks and he did not think that this could always be done with the Frejka pillow in active babies As regards splintage he believed that it should not be too rigid but should allow movement of the legs which should be held abducted in such a position that the head of the femur is centered towards the acetabulum The splint should not be left on for more than three months

Jacobsson mentioned that his patients had been treated with a slight modification of the von Rosen splint and that the splintage had probably been too rigid In view of the high incidence of secondary bone changes in his series less rigid splintage was now used

Lindstrom considered that the splint should be worn continuously It should not be removed for bathing the baby Within his region where the paediatricians had earlier had the care of the cases and issued instructions he had seen redislocations which he believed were attributable to the practice of frequent removal of the splint

Fellander asked von Rosen whether he believed that it was precarious to exclude certain cases from treatment as was done by Jacobsson s method Such a decision would require great *experience on the part of the examiner* and the policy should perhaps not be recommended for general use

von Rosen replied that it was difficult to decide which babies needed treatment and as for himself he did not want to take the risk of leaving a baby untreated

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SCHELLER described the routine in Gothenburg where the babies are examined by X-ray at birth, then at the age of six weeks and three months thereafter; repeated examinations are made if required depending upon the clinical course. When it is of interest to study the growth of the bone nucleus the X-ray examination is sometimes repeated.

RIBBING considered that too little is known about the hazards of X-ray examination and that the greatest caution should be recommended. This was the reason why, so far, he has not, unlike Andrén in Malmö, applied a more thorough examination schedule, but he will try it as he expects shortly to have at his disposal an X-ray apparatus which will permit substantial reduction of the dose by taking the pictures direct from an image intensifier with checking on the television screen.

ANDRÉN gave a report of the dose measurements made at the Institute of Radiophysics by which it has been found that the radiation dose for one exposure equals one week of background radiation, provided that the newborn infant is placed direct on the plate holder and that a high speed film and large film-to-tube distance are used. The risk of genetic injury is greater at X-ray of the pelvis in a 20 year old patient. The radiation in this case will be at least 100 times as high as that to the newborn baby. A newborn baby, if anybody, can be subjected to X-ray examination without any risk of genetic injury. This is because the dose to the gonads is so small in comparison with that used for larger objects. If we were to hesitate to use X-ray in examining the newborn we would not dare to make any X-ray examinations whatsoever.

4 Secondary bone changes

HIRSCH *referred to animal experiments which showed that an abnormal* position in the hip joint can result in disturbances of the growth of the nuclei and raised the question whether rigorous abduction treatment could involve the risk of such disturbances.

SEVASTIKOGLOU brought up the question of the association between the mode of immobilization and the occurrence of bone changes. In the Uppsala series a Frejka pillow was used exclusively. Osteochondrosis of the capitular epiphysis was seen in only one case. In the Stockholm series the infants were placed in a von Rosen splint and such changes were seen much more frequently.

FELLÄNDER drew attention to a study in children by Hnevkovsky and his co-workers, which was presented at a round table conference at the SICOT's congress in Paris 1966. The author observed cessation of arterial blood flow to the femoral head at extreme abduction.

VON ROSEN believed that the frog position is neither dangerous nor unphysiological in the first three months of life He was surprised at the numerous secondary bone changes that were seen in the Stockholm series and pointed out the necessity of finding the reason as well as the importance of a continuous follow up of all series

5 Missed cases

In this part of the discussion the subject was cases of hip dislocation which was not discovered by routine examination of the hip joint in the maternity departments As regards the diagnosis *Jacobsson* emphasized that the examination should be made with the baby lying flat on its face with a view to detecting any limitation of abduction If this was present particularly if it was noted on one side only dislocation of the hip could be strongly suspected With such an examination routinely of infants in their second or third month the number of missed cases of hip dislocation should be reduced If the hip cannot be abducted to about 60 an X ray examination should be performed and at this age it can give definite information as to the presence or absence of dislocation

As regards treatment FELLANDER stated that infants in whom the dislocation is detected at the age of three to six months should also be treated by mild reduction with traction in a position of abduction —inward rotation that is the method which nowadays is fairly generally recommended in reduction of dislocation in older children With this mild reduction the risk of circulatory disorders in the femoral head is smaller Manipulations under anaesthesia and immobilization in a frog position should therefore not be used Fellander mentioned that he had seen a patient whose dislocation was detected at the age of six months and who had been treated elsewhere in the ordinary frog position The dislocation could not be corrected in this position Arthrography with checking on the roentgen television screen showed that it became corrected when the leg was held in a position of abduction— inward rotation and dislocated in the frog position In such cases arthrography would be useful in showing how to adjust the leg to obtain a good position of the femoral head The examination must be carried out under anaesthesia but does not involve any traumatic manipulation The use of an image intensifier ensures a low radiation dose There is no reason to perform arthrography in uncomplicated cases The arthrographies in the Stockholm series were undertaken to display the anatomy in normal and pathological cases

VON ROSEN had very limited experience of missed cases In the Malmo series from 1952 1963 there were three cases in which dislocation was detected when the children had begun to walk He had personally treated

two of them by closed reduction under anaesthesia and subsequent immobilization in plaster by Lorenz s method The treatment had offered no difficulties The acetabular roof had developed satisfactorily in both cases and no epiphyseal damage had occurred The third case had been treated in the same way elsewhere But the acetabular roof had not developed equally satisfactorily but clinically the condition has been satisfactory up to now

Hirsch also uses traction as the primary measure If this fails open reduction is carried out by which he has found that the tendon of psoas acts as an obstacle to the reduction together with the joint capsule possibly the limbus The tendon of psoas is divided and on splitting the capsule it is found that the head of the femur can easily be made to slip into the acetabulum The psoas tendon is then transferred in front to the great trochanter thus assuming the ability of inward rotation If necessary a shelf operation is made in connection with the reduction

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The Rush brothers introduced in 1927 curved flexible solid steel pins for intramedullary osteosynthesis In the fixation of diaphyseal fractures with these pins an elastic three point fixation is produced which however often allows relatively large movements in the fracture line The mechanical stability of the osteosynthesis is often inadequate As a rule therefore further complementary external fixation is required

In 1940 Kuntscher introduced a new principle of osteosynthesis with a steel nail which was initially V-shaped but was later given the shape of a clover leaf The nail could be compressed elastically from the sides Kuntscher intended that it should be squeezed against the cortex inside the medullary cavity In order to obtain stable fixation the nail has to be pressed firmly in the medullary cavity in both the proximal and distal fracture fragment With hour glass shaped medullary cavities this means that the nail gives adequate fixation only in relatively transverse fractures within the narrowest area of the diaphysis

Rigid fixation preferably stable enough for weight bearing, gives important advantages by allowing earlier mobilization of the patient and thus more rapid restoration of the general state of health with a decreased risk of thrombosis and renal calculi as a result. As regards local conditions of the affected limb there will be reduced muscular atrophy reduced periarticular fibrosis and oedema and more rapid removal of breakdown products from the fracture region

In order to increase the possibilities of osteosynthesis of diaphyseal fractures with an intramedullary nail sufficiently stable for weight bearing Küntscher developed in 1950 hand-operated reamers for widening the medullary cavity and in 1954 electrically driven reamers on a flexible axis which can be threaded over a guide wire which is inserted into the medullary cavity By enlarging the medullary cavity space is created for a nail of such a diameter that it can take up the mechanical forces when weight is placed on the limb In this way the risk is also avoided of the nail becoming wedged in the medullary cavity and splitting the cortex or separating

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the fracture fragments by wedging in the distal fragment By enlarging the medullary cavity in the middle part of the bone the nail can be held fast along a greater proportion of its length than is otherwise possible Less force is required for driving home the nail, which probably means a reduced risk of fat embolism

The pressure conditions in the distal metaphysis of the tibia were studied by Wehner (1968) with closed reaming and nailing of fractures of the tibial diaphysis in man He found that 5–8 days after the fracture the medullary cavity pressure was 9–10 mm Hg When the medullary cavity was opened with an awl, its pressure rose to 20–25 mm Hg within a short time Closed reduction resulted in the same degree of pressure increase When the guide wire was first inserted in the medullary cavity a pressure increase of about 40 mm Hg was obtained On subsequent reaming there was a maximal pressure increase of 120 mm Hg The pressure increase was greatest when the reaming began in the distal fragment and was greater the wider the calibre of the reamer When the reamer was withdrawn from the medullary cavity, a negative pressure of about 100 mm Hg was recorded On driving in the nail, practically no measurable pressure increase was obtained With an open operation on the fracture a smaller pressure increase was obtained than with a closed technique Operations on the femur gave similar results to those on the tibia

Since 1964 we have employed Kuntscher s instrument for reaming of the medullary cavity and have now used it on about 30 fresh fractures of the femur and in a few pseudarthroses After about 1 week of preoperative extension therapy the operation was performed on an extension table under radiographic control with a television monitor For two reasons the fracture was reduced by the open technique through an incision lateral to vastus lateralis firstly to provide a possibility of more exact reduction and secondly to counteract the pressure increase in the medullary cavity and in the fracture haematoma associated with the reaming of the medullary cavity The medullary cavity was reamed from the tip of the greater trochanter using short reaming stages and with the least possible pressure against the reamer The calibre of the reamer was increased step wise by $^1/$ –1 mm each time from 10 mm The reaming was discontinued when both fracture fragments had been adequately reamed A nail of greater diameter than 11 5 mm and $^1/$ –1 mm narrower than the widest reamer was chosen The length of the nail was determined by measurement on the television screen of the guide wire which had been inserted in the medullary cavity on reaming In fractures on the distal part of the middle third of the bone the nail was inserted to about 1 cm above the intercondyloid fossa to be secured there in the cancellous bone Proximally the nail should extend no higher than to

about 1/ cm above the tip of the trochanter Large intermediate fragments were secured to the bone by cerclage and the cerclage wires were removed within 3–4 *months after the operation* The periosteal blood supply of the intermediate fragment was maintained as far as possible The clinical results of the operations have been promi ing The main advantage of the method namely that the patient can usually put full weight on the limb within 2 weeks postoperatively has been fully utilized A more detailed report of the clinical results will be published elsewhere

The periosteal cuff of callus was always everal cm wide and the callus mass was assessed as considerable Periosteal callus was visualized as a thin cloud like shadow 3–4 weeks after the operation The callus tissue showed its maximal extent on the radiograph about 6 weeks after the operation After this time there was usually no increase in the amount of callus

Within the area in the vicinity of the fracture *where* by *reaming* the cortex had become greatly thinned—in some ca es to half of its previous thickness—the periosteal callus tissue does not at first become attached to the thinned bone but bridges this area An area of low density is then seen on the radiograph betw en the callus tissue and the underlying bone which is probably totally avascular and necrotic After *ome months this* bone be comes clearly eroded from the p rio teal sid- and seems to be largely re placed by periosteal callus

An intermediate fragment in which the periosteal circulation is retained and which is fixed into the osteosynthesis by cerclage is covered by a large amount of periosteal callus which seems to become *attached to the fragment* from the beginning except within a narrow zone nearest to the fracture gaps This finding is considered by Charnley (1968) to be a sign of ischaemia of the fracture ends

In some younger patients the periosteal callus formation was not only localized to the fracture area but was also fourd as a *thin cuff* of bone around the greater part of the diaphysis

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The following factors oppose the view that in this material the development of periosteal callus was due essentially to instability

1 The callus tissue was already of the same extent when it first became visible radiographically after 3–4 weeks No gradual increase, of the type seen in the development of a hypertrophic pseudarthrosis, was observed

2 No line of low density passing through the entire periosteal callus cuff was seen, as can be observed when there is considerable instability in a fracture

3 No bone resorption around the nail occurred until the fracture had healed

4 The patients were already free from pain in the fracture area about 1–2 days after the osteosynthesis

Reports have been published of several experimental studies on the reaction of the long bone after Kuntscher nailing and after evacuation of the medullary cavity On the other hand no studies appear to have been made of the reaction of the long bone to the removal of bone from the endosteal surface by reaming of the medullary cavity

The aim of the present investigation was to study, by means of Indian ink angiography, bone labelling with tetracycline and histological methods the effect of reaming of the medullary cavity on the formation of callus and on the microcirculation in order to obtain an idea of the conditions of healing with this method of treatment To investigate the effect *per se* the study was made of reaming of the medullary cavity of non fractured long bones

CHAPTER 1

Review of Literature

THE NORMAL VASCULAR SUPPLY OF THE TIBIAL DIAPHYSIS IN THE RABBIT

The investigations of Langer in 1876 and the angiographic studies of Lexer et al in 1904 provided the basis for our understanding of the arterial vascular supply in the bone The anatomy of the larger vessels is now well known while the microcirculation of the cortex is still obscure in many respects

The diaphysis of the long bone obtains its arterial blood supply from three sources namely the nutrient artery the metaphyseal arteries and the periosteal arteries The nutrient artery of the tibia in the rabbit arises from the anterior tibial artery and perforates the tibia on the fibular side about 5 mm above the tibiofibular synostosis (Brookes & Harrison 1957 Gothman 1961) The artery passes obliquely through the cortex of the tibia in the distal tibial direction without giving off any branches to the cortex during its transit (de Marneffe 1953 Brookes 1964) In the medullary cavity the nutrient artery divides into ascending and descending branches which anastomose with the metaphyseal vessels (Gothman 1961) Branches from the nutrient artery supply the bone marrow To the cortex pass both relatively wide arterioles which penetrate half the cortex and anastomose with vessels in the Haversian systems (Brookes 1964) and branches which penetrate the innermost layer of the cortex then to return to the medullary cavity and empty into venous sinusoids (Rohlich 1941 Brånemark 1959) In addition to these vessels there are branches which penetrate the entire cortex and directly connect the periosteal arterial system with the nutrient artery without interceding capillaries (Brookes & Harrison 1957 Gothman 1961) In practically all cases there is a secondary nutrient artery even though rudimentary (Gothman 1961) This perforates the tibia ventro-distally to the tibiofibular synostosis and supplies the fibular distal part of the tibial medullary cavity Sometimes the descending branch of the primary nutrient artery is lacking In these cases branches from the secondary nutrient artery supply the whole of the medullary cavity distal to the synostosis

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anastomose with branches of the nutrient artery, resulting in the formation of a medullary arterial system (Brookes & Harrison, 1957, Gothman, 1961, Trueta & Caladias 1964) The growing epiphysis has a separate vascular supply After closure of the epiphysis anastomoses occur between the metaphyseal and the epiphyseal arteries (Trueta & Caladias, 1964) According to Gothman (1961) the anastomoses with the vessels in the distal epiphysis are wide but narrow with the vessels in the proximal epiphysis

The periosteal arterial system of the diaphysis consists of six or seven longitudinal artieries, which run along the entire length of the diaphysis and unite the arterial periosteal plexus at the metaphyses (Morgan 1959) In growing bones branches pass from the periosteal arteries to a capillary network located in the osteogenic layer of the periosteum immediately adjacent to the bone surface (Brookes 1964) This periosteal capillary net work is in addition supplied with a large number of small vessel branches from musculature attached to the bone The periosteal capillary network communicates with the vessels in the Haversian canals via several narrow vessels which arise from the network almost at right angles These vessels which penetrate the outer cortex are most profuse nearest to the metaphyses (Morgan 1959 Trueta 1963, Gothman 1961)

The main venous vessel in the rabbit tibia consists of a thin walled canal located in the centre of the medullary cavity This canal is about 10 times wider than the nutrient artery (Brookes 1964) According to Morgan (1959) there are two principal veins in the distal part of the tibia which unite just below the middle of the tibia From this central vein radiate like spokes of a wheel a large number of venous sinusoids into which intracortical veins and medullary vessels empty The central vein is emptied partly through an emissary foramen situated inferio anteriorly to the entrance of the secondary nutrient artery and partly through several small veins especially in the metaphyseal areas, to veins outside the bone

The vessels in the diaphyseal cortex lie in bone canals the diameters of which are 10–20 μ (Branemark, 1959) Brookes (1964) states that within the periosteally formed bone in young adult rabbits the bone canals con verge towards the primary ossification centre of the shaft In the endochon drally formed bone the bone canals show a mainly longitudinal course Numerous transverse anastomoses are found between the bone canals The intracortical canals tend to be wider towards the endosteal than towards the periosteal surface (Cohen & Harris 1958) The bone canals usually contain one vessel which consists of a single endothelial tube of constant diameter even after repeated divisions and anastomoses (Brookes 1964) According to Branemark (1959) the diameter of this capillary is 7–8 μ On vital microscopy of the endosteal part of the cortex in the rabbit fibula

Branemark (1959) found in some intracortical canals two vessels with different flow rates and opposite flow directions Trueta (1963) found on ultraviolet microscopy of subperiosteal bone from the rabbit after injection of tetracycline intracortical canals containing two vessels one of which he considered to be a precapillary and the other a vein Brookes (1964) observed further that in the endosteal part of the cortex there was a relatively small number of wide canals which contained precapillaries

There is disagreement between different investigators as to which parts of the diaphyseal cortex in the rabbit are normally supplied by the different arterial systems The various observations have been made by histological and angiographic studies (de Marneffe 1951 1953 Brookes & Harrison 1957 Morgan 1959 Gothman 1961 Trueta 1963 Trueta & Caladias 1964) and by vital microscopic investigations (Brånemark 1959) The circulation in the cortex is described by Brookes (1964) as mainly centrifugal According to Brookes the cortex is supplied with blood from branches of the nutrient artery in the medullary cavity which penetrate half the cortex and anastomose there with the capillary system in the Haversian canals Depending upon the pressure conditions in the medullary cavity and in the veins outside the bone the blood flows from the central parts of the cortex in a centrifugal direction to the periosteal vessels or in a central direction to the venous system of the medullary cavity According to Rohlich (1941) the majority of the veins of the compact bone empty into the sinusoids of the medullary cavity

The vessels in the subperiosteal bone are considered by Brookes (1964) to be solely efferent veins This opinion is shared by Brookes & Harrison (1957) McAuley (1958) Macnab (1958) Gustilo *et al* (1964) and Harrison (1966) and is based principally on angiographic studies using a suspension of fine grained barium sulphate (Mikropack) as contrast medium According to Brookes & Harrison (1957) however Mikropack does not fill the vessels distal to the arterioles This means that the capillaries leading from the periosteum into the cortex often remain empty of the perfusion medium (Trueta 1963) Morgan (1959) and Trueta (1963) consider that the outer one third of the cortex is supplied by periosteal vessels and the inner two-thirds by branches of the nutrient artery De Marneffe (1953) claims that the cortex in the upper part of the tibial diaphysis in the rabbit is supplied mainly from medullary vessels and that in the middle part from both periosteal and medullary vessels while in the distal part of the diaphysis the vascular supply takes place almost exclusively from periosteal vessels Communications between the periosteal and endosteal vascular systems via vessels which are wider than capillaries and which pass through the entire cortex have been shown by Brookes & Harrison (1957) Morgan (1959)

Gothman (1961) Trueta & Caladias (1964), Brookes (1964) and Rhinelander *et al* (1968), among others

From angiographic studies in the rabbit, Koekenberg (1963) summarizes the intracortical circulation as follows the cortical network can be considered the capillary system of both the periosteal and the marrow vessels The cortical network itself forms an anastomosis between periost and marrow vessels" He considered the most important source of blood supply to be the nutrient artery however This opinion is shared by Rhinelander *et al* (1968), Kelly (1968) and others

THE EFFECT OF SELECTIVE OCCLUSION OF THE MAIN BLOOD VESSELS OF THE LONG BONE ON THE INTRACORTICAL AND MEDULLARY CIRCULATION

The long bone obtains its arterial blood supply from three vascular systems the nutrient artery the metaphyseo-epiphyseal arteries and the periosteal vessels For understanding of the nutrition of bone after operations on the diaphyseal cortex, it is essential to know to what extent the different vascular systems can take over each others normal supply areas Attempts have been made to clarify this question by selectively occluding in animals one or more of the vascular systems and then studying by histological and angiographic methods the extent of the necrosis which has occurred and the deficiency of vascular visualization in the tissue Pressure measurements in the medullary cavity have also been made in an attempt to elucidate this problem

Division of the Nutrient Artery

The nutrient artery has been divided outside the bone For the blood supply to the bone, the periosteal and the metaphyseo-epiphyseal vessels then remain Such studies were performed on the rabbit by Bragdon *et al* (1949) and by Trueta & Caladias (1964) On histological examination Bragdon *et al* found in the femur of young rabbits small areas of infarction in the medulla and also in the inner parts of the cortex In some cases large areas of cortical necrosis were found Trueta & Caladias studied the radius in young and adult rabbits by histological methods and by angiography with Mikropack They reported normal visualization of the vessels in the medulla and cortex and histologically no necrosis was seen either in young or adult animals

Ligation of the nutrient artery outside the bone was performed in the dog

tibia by Drinker *et al* (1922) On perfusion of the remaining vessels with Indian ink normal visualization of the intracortical and medullary vessels was obtained

Shaw (1964) ligated the nutrient artery in the femur of young cats with open epiphysis and found a pronounced fall in the intramedullary pressure and blood flow while in adult animals the operation resulted in only a slight reduction of the intramedullary pressure and blood flow Cuthbertson *et al* (1964) reported that ligation of the nutrient artery of the tibia and humerus in dogs caused an immediate and profound fall in the intramedullary pressure and it remained low for 1–3 hours in 9 out of 19 bones and for 4–22 days or more in the 10 other bones

Division of the Nutrient Artery Combined with Blockade of the Periosteo Cortical Circulation

After division of the nutrient artery and occlusion of the periosteal and cortical vascular communications only the metaphyseo-epiphyseal vessels remain for providing the arterial blood supply The function of the periosteal vessels will have been temporarily discontinued by the fact that the periosteum is lifted up from the cortex and then replaced against it Revascularization of the cortex from the periosteum is then not prevented Permanent occlusion of the periosteo-cortical communication has been brought about by placing teflon foil between the periosteum and bone after raising the periosteum from the cortex the teflon foil then preventing revascularization of the cortex from the periosteum Such studies have been performed on the rabbit by Foster *et al* (1951) and Trueta & Caladias (1964) After temporary occlusion of the periosteal circulation and division of the nutrient artery Foster *et al* found in the femur of young rabbits on histological examination total necrosis of both the bone marrow and the cortex In adult animals they obtained very varying results Thus in many animals both the bone marrow and the cortex remained normal Trueta & Caladias found in young rabbits after permanent occlusion of the communications between periosteum and cortex with division of the nutrient artery that the nutrient artery in the medullary cavity did not fill with Mikropack on angiography and that histologically there was total necrosis of both the bone marrow and the cortex In adult rabbits the nutrient artery filled with contrast medium inside the medullary cavity The bone marrow remained normal histologically but the outer and middle parts of the cortex became devitalized

Corresponding studies were performed on the dog by Johnson (1927) Brunschwig (1929) Larson *et al* (1961) and Silberman *et al* (1967) After

temporary occlusion of the periosteo cortical vascular communications and division of the nutrient artery in young dogs, Brunschwig found necrosis of the bone marrow and inner parts of the cortex on histological examination Larson *et al* found almost complete filling of the intramedullary vessels with Mikropack on angiography and a fully viable cortex histologically, and Silberman *et al* observed almost total avascularity of the cortex on angiography with Mikropack seven days after the operation but a viable cortex on histological studies This might be due to factors discussed on page 74

After permanent occlusion of the communications between periosteum and cortex and simultaneous division of the nutrient artery in young dogs Larson *et al* found that in some cases the bone marrow lacked Mikropack filled vessels while in other cases the vascular visualization was increased The cortex remained viable in some cases, and was necrotic or partially necrotic in others Silberman *et al* observed total necrosis of the bone marrow and cortex

On temporary occlusion of the periosteo cortical communications and division of the nutrient artery in adult dogs Brunschwig and Larson *et al* found no damage to the bone marrow or cortex On permanent occlusion of the periosteo-cortical communications and division of the nutrient artery also in adult dogs Larson *et al* observed some necrosis of the bone marrow while Silberman *et al* and Johnson found the marrow to be normal Larson *et al* and Silberman *et al* both found a normal cortical circulation while Johnson observed necrosis of the outer two thirds of the cortex

Blockade of the Periosteo Cortical Circulation

After blockade of the periosteo cortical circulation the nutrient artery and the metaphyseal vessels remain for vascular supply of the cortex Trueta & Caladias (1964) found partial necrosis of the outer parts of the cortex *after permanent blockade of the periosteo* cortical circulation in the rabbit tibia The bone marrow and remaining parts of the *cortex remained viable*

Blockade of the Periosteo Cortical Circulation and of the Metaphyseal Vessels

After blockade of the periosteo cortical vascular communications and of the metaphyseal vessels the nutrient artery is solely responsible for supplying the diaphysis The metaphyseo—epiphyseal vessels have been blocked by opening the medullary cavity in the metaphyses and scraping out the bone marrow In order to obtain permanent blockade of the metaphyseal vessels the medullary cavity has been plugged with *for example* wax in the metaphyseal area

After permanent blockade of the metaphyseal vessels in this way and permanent occlusion of the periosteo-cortical vessels with interposition of teflon Trueta & Caladias (1964) found normal visualization of the vessels of the bone marrow and of the inner /3–3/4 of the cortex on angiography with Mikropack in tibiae of both young and adult rabbits The vessels in the outer 1/3–1/4 of the cortex did not fill with Mikropack and these parts of the cortex showed necrosis Johnson (1927) after similar operations on the dog observed necrosis of the outer two-thirds of the cortex but otherwise normal cortex and medullary contents

The function of the nutrient artery can also be studied by perfusion of the vessel Perfusion with Indian ink of the nutrient artery alone without interference with the remaining vascular systems was performed by Drinker *et al* in 1922 After this procedure they obtained visualization of the entire cortical and medullary vascular systems and noted that Indian ink left the bone through periosteal vessels Shim *et al* (1968) found on studying the arterial supply of the femur in young rabbits with strontium[8] that the nutrient artery was responsible for 71 / of the blood supply to the diaphysis including the bone marrow

Division of the Nutrient Artery and Occlusion of the Metaphyseal Vessels

The possibility of the periosteal arteries to compensate for loss of the nutrient artery and metaphyseal vessels is of especial interest with regard to operations in the medullary cavity Different investigators have obtained very divergent results in such studies which has probably been largely due to the different methods used Trueta & Caladias (1964) divided the nutrient artery outside the tibia in young and adult rabbits and at the same time made a permanent break in the communication between the metaphyseal and diaphyseal vessels within the medullary cavity by scraping out the bone marrow in the metaphysis and plugging the cavity with wax They found that on angiography with Mikropack the intracortical vessels were not visualized until about one week after the operation and also that the bone marrow and inner two-thirds of the cortex had become necrotic Macnab (1958) McAuley (1958) and Gustilo *et al* (1964) considered after perfusion studies with Mikropack that the periosteal vessels were unable to supply any part of the cortex Johnson (1927) found after obliteration of the medullary circulation in the tibial diaphysis of the dog that total necrosis of the bone marrow had occurred and necrosis of the inner half of the cortex He also found that on Indian ink angiography the cortex was very little injected De Marneffe (1951) claims that the periosteum in the distal part

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is no definite evidence that the periosteal vessels cannot take over the nutrition in part of the diaphyseal cortex

There seems thus to be no marked difference between the rabbit and dog with regard to the potentialities of the three different vascular systems for taking over each others circulatory regions

THE EFFECT OF SURGERY ON THE MEDULLARY CAVITY OF THE DIAPHYSIS OF THE LONG BONE

Partial Destruction of the Medullary Circulation

Surgery to the medullary cavity can disturb the medullary and cortical circulation to different degrees On intramedullary nailing of the rabbit tibia *without fracture* Gothman (1961) found that remnants of the nutrient artery were often visualized in the medullary cavity on arteriography During the first days after the operation he observed slight filling of the intracortical vessels with Mikropack contrast medium Not until after 10 day were the intracortical vessels better visualized The osteocytes in the cortex remained viable

Trueta & Cavadias (1955) studied fractured radii in rabbits treated with intramedullary nailing and found on angiography with Mikropack that the medullary vessels were practically always completely destroyed Even far from the fracture line necrosis of the inner third to two thirds of the cortex was observed histologically in both young and adult animals

On intramedullary nailing of osteotomized rabbit tibiae Gothman (1961) often found remnants of the medullary arteries in the medullary cavity The vascular filling in the cortex away from the fracture line was similar to that in tibiae subjected to intramedullary nailing but not fractured In two out of 35 rabbits a long irregular area of periosteal callus was seen along both fracture fragments On angiography of osteotomized tibiae in rabbits treated with intramedullary nailing using Mikropack+Berlin blue as contrast medium Koekenberg (1963) obtained a similar degree of visualization of the medullary vessels as Gothman (1961)

Rhinelander *et al* (1967) performed osteotomy and intramedullary nailing of the ulna in dogs and found on angiography with Mikropack that the cortex in contact with the medullary nail showed reduced vascularity of the inner half to two-thirds while that which had no contact with the nail was vascularized

Gustilo et al (1964) found on Mikropack angiography of osteotomized dog femurs treated with intramedullary nailing that the periosteal vessels did not penetrate the cortex to supply it

of the rabbit tibia can supply the entire cortex Rhinelander & Baragry (1962) consider that the periosteal circulation of long bones can take over when the medullary circulation has been interrupted

Summary

The diaphysis of the long bone is *supplied from the nutrient artery,* the metaphyseal and the periosteal arteries If one or more of these arteries is obliterated the remaining vessels will to varying extents take over their function

The periosteal and the metaphyseo epiphyseal vessels are able together to supply both the bone marrow and the cortex when the nutrient artery has been divided In growing animals the periosteal arteries are then of the greatest importance, while in adult animals, in which the epiphysis is closed, the most important vessels are the metaphyseal and epiphyseal arteries (Trueta & Caladias, 1964)

In young rabbits the metaphyseal vessels cannot alone supply the con *tents of the medullary cavity and the cortex even if revascularization of the* cortex from the periosteum is not prevented In young dogs the metaphyseal vessels protect the cortex from necrosis if revascularization from the perio steum is not rendered impossible but if revascularization is prevented varying degrees of cortical necrosis occur In both adult rabbits and adult dogs the metaphyseo epiphyseal vessels alone can essentially supply the contents of the medullary cavity and at least the inner parts of the cortex

If only the nutrient artery remains and the periosteo-cortical circulation is permanently interrupted necrosis occurs in the outer third of the cortex but when teflon foil is interposed between the periosteum and cortex the venous outflow from the cortex is probably also affected and this can contribute to the cortical damage Rhinelander *et al* (1968) has pointed out that a blocked cortical outflow can cause the occurrence of bone necrosis under a compression plate lying closely against the bone

In cases where the periosteal vessels alone remain several investigators have found that the intracortical vessels are not visualized primarily on angiography with Mikropack This has been considered to mean that no functioning vessels are present Trueta (1963) pointed out however that a lack of visualization of the vascular system with Mikropack does not preclude the presence of a nutritive flow When the medullary cavity of the metaphyses were plugged with wax in order to close off the metaphyseal circulation a pressure increase may have been produced in the medullary cavity which might have affected the circulation in the cortex Thus there

dullary vessels The bone formation was most extensive over the areas where the medullary and intracortical circulation was most severely damaged (Axhausen & Bergmann 1937 Trueta & Cavadias 1955 de Marneffe 1951 Gustilo *et al* 1964 Richany *et al* 1965 Andersson 1965 Mital & Cohen 1966) Richany *et al* found that the amount of periosteal bone formation corresponded exactly with the extent of medullary removal The increased subperiosteal bone formation has been considered by Kuntscher (1957) to be due to local acidosis and by Trueta & Cavadias to periosteal hyperaemia over necrotic cortex Richany *et al* and Johnson (1966) considered that local stasis with oedema and periosteal anoxia was the cause of the periosteal bone formation while Zucman *et al* (1968) showed that medullary fragments were squeezed out through the cortex to the subperiosteal space and there gave rise to extensive formation of bone

The subsequent development of the periosteal callus tissue has been studied by Trueta & Caladias (1964) Richany *et al* (1965) and Zucman *et al* (1968) Trueta & Caladias found in young rabbits that the subperiosteal cells proliferated after 2 days that new bone was present after 4 days and that after 6 days there were new trabeculae subperiosteally After 12 days the new bone covers the whole ulnar surface of the radius In adult rabbits a thin smooth layer of lamellar bone was found subperiosteally after 6 weeks Richany *et al* observed in young adult cats early marked cellular proliferation with circumferential subperiosteal bone deposition involving the diaphyses A maximal amount of subperiosteal bone was seen after an observation time of 20 days and subsequently the bone mass gradually decreased Periosteal bone was transformed to mature Haversian compact bone

Zuchman *et al* (1968) studied growing rabbits after reaming of the medullary cavity without removing bone from the endosteal surface They found on radiographic examination that callus tissue was observed 15 days postoperatively and this tissue reached a maximal size on the 15th to 21st day In the centre of the callus cavities developed and in the periphery of the callus corticalization was observed Cavities in callus tissue were described by Falkenberg (1961) in osteotomies with intramedullary nailing in rabbits He observed the first cavity 30 days after the operation According to his photographic illustrations it would seem that the cavities were localized more and more centrally in the bone with increasing time postoperatively

Cortical Reaction

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Gothman (1961) performed intramedullary nailing of osteotomized tibiae in monkeys He found on angiography with Mikropack that the medullary arteries were less extensively damaged than in the rabbit In monkeys also, he observed almost no filling of the intracortical vessels with contrast medium during the first week postoperatively

Intramedullary nailing of osteotomized long bones in animals without angiographic examination has been performed by several investigators including Kuntscher (1961) and Anderson (1965)

Total Destruction of the Medullary Circulation

If the medullary contents are removed the cortex is completely dependent upon the periosteal circulation for its nutrition Such operations have been carried out on rabbits by Rohlich (1941) Branemark (1964) and Zucman *et al* (1968), on cats by Richany *et al* (1965) and on rats by Mital & Cohen (1966) In connection with this operation angiography has only been performed by Mital & Cohen Rohlich removed the bone marrow of the diaphysis with gauze after dividing the bone through the metaphyses Branemark removed the marrow through a groove sawn out on the anterior side of the bone Richany *et al* washed out the marrow with salt solution and, after having put down a rotating stainless steel pin in the cavity brushed the medullary cavity with a pipe cleaner He obtained massive necrosis of the cortex except within the very outermost layer Mital & Cohen removed the medulla by several different methods including suction brushing with a baby-bottle brush and filling of the medullary cavity with agar, and found necrosis in the cortex on maximal injury

After operations in the medullary cavity with partial or total destruction of the bone marrow typical reactions from the periosteum cortex and medullary cavity are obtained

Periosteal Reaction

On disturbance of the endosteal circulation the periosteum reacts with increased vascular filling and proliferation of the vessels (Trueta & Cavadias, *1955 Gothman 1961* Zucman *et al* 1968) Trueta & Cavadias consider that proliferation of the periosteal vessels is always accompanied by the formation of new bone Despite considerable vascular proliferation in the periosteum after intramedullary nailing of non fractured tibiae in rabbits Gothman found no new bone formation in the periosteum however except in a very few cases

Increased periosteal new bone formation in the diaphysis of the long bone has been demonstrated by several investigators after destruction of the me

dullary vessels The bone formation was most extensive over the areas where the medullary and intracortical circulation was most severely damaged (Axhausen & Bergmann 1937 Trueta & Cavadias 1955 de Marneffe 1951 Gustilo *et al* 1964 Richany *et al* 1965 Andersson 1965 Mital & Cohen 1966) Richany *et al* found that the amount of periosteal bone formation corresponded exactly with the extent of medullary removal The increased subperiosteal bone formation has been considered by Kuntscher (1957) to be due to local acidosis and by Trueta & Cavadias to periosteal hyperaemia over necrotic cortex Richany *et al* and Johnson (1966) considered that local stasis with oedema and periosteal anoxia was the cause of the periosteal bone formation while Zucman *et al* (1968) showed that medullary fragments were squeezed out through the cortex to the subperiosteal space and there gave rise to extensive formation of bone

The subsequent development of the periosteal callus tissue has been studied by Trueta & Caladias (1964) Richany *et al* (1965) and Zucman *et al* (1968) Trueta & Caladias found in young rabbits that the subperiosteal cells proliferated after 2 days that new bone was present after 4 days and that after 6 days there were new trabeculae subperiosteally After 12 days the new bone covers the whole ulnar surface of the radius In adult rabbits a thin smooth layer of lamellar bone was found subperiosteally after 6 weeks Richany *et al* observed in young adult cats early marked cellular proliferation with circumferential subperiosteal bone deposition involving the diaphyses A maximal amount of subperiosteal bone was seen after an observation time of 20 days and subsequently the bone mass gradually decreased Periosteal bone was transformed to mature Haversian compact bone

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the viable outer part of the cortex (Phemister, 1930 Rohlich, 1941 Trueta & Cavadias, 1955, Kockenberg 1963 Ricany *et al* 1965, Rhinelander *et al* 1968) The channels in the viable part of the cortex become wider and contain more blood vessels (Axhausen & Bergmann, 1937 Brookes, 1960) Vessels with preceding osteoclasts, so-called cutting heads, bore channels through the necrotic bone in the direction towards the medullary cavity The bone channels then become gradually narrower behind the cutter head by the formation of bone on their walls (Schenk & Willenegger, 1963, Johnson 1966) In young animals, large, irregular resorption cavities can be formed in the necrotic bone (Axhausen & Bergmann, 1937, Richany *et al* 1965) but in adult animals small round cavities are formed (Johnson 1966) This rebuilding process also affects viable bone but the resorption cavities are smaller in viable than in necrotic bone (Axhausen & Bergmann, 1937)

In young adult cats the maximal reconstruction of the cortex takes place 40 days after disturbance of the endosteal circulation when the periosteal reaction is already declining (Richany *et al* 1965) Trueta & Cavadias (1955) found that in growing rabbits cortex two-thirds of which had primarily shown necrosis, was almost completely rebuilt after 7 weeks, while in adult animals necrotic areas were still present after 8 months Resorption in the inner part of the cortex was established radiographically after an observation time of 4 weeks (Trueta & Cavadias, 1955, Richany *et al* 1965) According to Phemister (1948) large necrotic areas in the cortex are never completely rebuilt Especially in older individuals, the reparative stimulus seems to become exhausted Axhausen & Bergmann (1937) consider that the cells from which new bone formation occurs in the necrotic bone areas arise from the periosteum or from the medullary cavity, while in the opinion of Trueta (1963) they arise from the vascular endothelium Other authors believe that the source of origin is the perivascular mesenchymal tissue (Brookes 1960) The amount of new bone that is formed to replace the degenerated necrotic bone is highly dependent upon the functional stimulus to which the limb is subjected (Phemister 1930) As a rule more bone is broken down within the zone than is reformed (Axhausen & Bergmann 1937)

Medullary Reaction

The healing processes in the medullary cavity after the evacuation of its contents have been studied by Rohlich (1941) Trueta & Caladias (1964) Branemark (1964) and Richany *et al* (1965) among others All these investigators give similar descriptions for these processes but the time course varies considerably After 3 days Branemark observed widening of the Haversian canals nearest to the medullary cavity and at the same time the

haematoma in the medullary cavity began to be organized Rohlich using histological methods observed bone formation in the medullary cavity after 14 days Trueta & Caladias noted some new vessels in the medullary cavity 9 days after operation Rohlich found that the bone bridges began to be resorbed within its peripheral areas 19 days after operation Branemark observed this 3 weeks after operation According to Richany *et al* the normal medullary structures were rebuilt after 160 days Rohlich observed that the vessels in the medullary cavity nearest to the residual avascular re gion were narrow while those around the bone bridges in the more peri pheral area of the medullary cavity were wide and thin walled Trueta & Ca ladias found that in adult rabbits blood vessels did not invade the medullary cavity from the cortex until after 6 weeks and infarctions still persisted in the medullary cavity 6 months postoperatively

HISTOLOGICAL CHANGES ON NECROSIS OF CORTICAL BONE

When the blood circulation to bone tissue is occluded the bone dies in the course of a few days (Phemister 1948 Bonfiglio 1954) Woodhouse (1962) after occlusion of the circulation to the femoral head for 6 hours in the dog found total necrosis of the femoral head in 3 cases out of 6 After occlu sion of the circulation for 12 hours he found total necrosis of the femoral head in all cases

Axhausen & Bergmann (1937) studied the development of bone necrosis and found that during the first week after the circulation to the cortical bone had been occluded no histologically visible changes occurred Later there was pyknosis of the osteocytic nuclei which became fragmented de creased in size and stained darker Axhausen & Bergmann considered that the recognition of pyknosis was rather difficult and required high magnifica tion and very careful observation They also considered that the most reli able sign that the bone was necrotic was the pre ence of nucleus free osteo cytic lacunae According to Axhausen & Bergmann the degeneration and removal of the pyknotic nucleus demands circulating tissue fluid The time it takes for the osteocytic nuclei in cortical bone to dissolve is dependent upon the thickness of the bone tissue and the penetration capacity of the ves sels which force their way in and by which means the dissolution takes place According to Schenk (1969) osteocytic nuclei in cortical bone disappear about 2 weeks after bone necrosis In dead bone the nuclei disappear first from the surface and the layer beneath contains pyknotic osteocytic nuclei (Axhausen & Bergmann 1937) In ischaemia of cortical bone without total occlusion of the circulation the cells in the interstitial lamellae to which

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Reaming, Brushing and Suction of the Medullary Cavity of the Rabbit Tibia

Material and Methods

Adult and growing non pregnant rabbits of different breeds and of both sexes were used for the experiments The rabbit was cho en as the main experimental animal both becau e its tibia is sufficiently large to allow reaming of the medullary cavity and because a relatively large number of animals was required

The information given by the breeders on the ages of the animals was not always reliable The material was therefore divided into two groups of adult and growing animals according to whether the fibular epiphysis was found to be closed or not on radiographic examination which was performed at the end of the experiment According to Heikel (1960) the epiphysis of the rabbit fibula closes at the age of 5–7 ¹/ months and according to Geiser (1963) this takes place at 5 months

Of 178 rabbits used 4 were used for determining the heat development and pressure conditions in the medullary cavity on reaming and brushing 22 for a study of intracortical fat and 24 for correlation of the amount of newly formed bone to the degree of traumatization of the cortex From the remaining 128 animals which were used for general morphological studies after reaming 25 were excluded after fracture had occurred on the treated leg and 17 died for various reasons during the experimental period The remaining 86 animals are presented in Table I

Preliminary studies showed that the morphological changes which occurred could most suitably be recorded at observation times of 3 days and 1 2 4 8 and 12 weeks Large groups of animals were therefore studied at these observation times after operation and these were called the main experimental groups In 61 of the 86 animals (28 adults and 33 growing animals) the medullary cavity of the left tibia was reamed while the right tibia served as a control In order to obtain a larger amount of material for morphological studies both the left and right tibia were reamed in 25 animals (7 adults and 18 growing animals) In these cases the left tibia was used for fluorescence microscopic studies and the right tibia for angiographic and histological studies

the nutrition is normally poorest die first, while the cells in the Haversian systems are still intact (Brookes 1960) On further deterioration of the blood supply the osteocytes in the remaining parts of the bone die, while the cells in the bone marrow and in the periosteal soft tissues can remain viable The osteocytes are thus very sensitive to anoxia (Halshofer 1937)

Bonfiglio (1954) found stainable osteocytic nuclei in the femoral head of the dog 2–3 weeks after total permanent occlusion of the circulation to the femoral head Catto (1965) obtained similar results in studies of the femoral head in man after medial femoral neck fractures, and Rokkanen *et al* showed in 1965 that histologically visible changes in the rabbit femoral head did not occur until 2–3 weeks after total occlusion of the circulation to the head

Other workers have found considerably more rapid removal of the osteocytic nucleus from necrotic cortical bone than the investigators referred to above Ham & Harris thus found in 1956 in fractures of cortical bone that the osteocytic lacunae at the fracture ends were already empty 2–3 days after the fracture Foster *et al* (1951) after ligation of the nutrient artery and stripping of the periosteum in the rabbit observed that the osteocytes in the cortex had faded already within the first 24 hours Within 3 days the osteocytic nuclei had disappeared except in some areas

Operation

The rabbits were anaesthetized with Nembutal® Abbot for veterinary use in a dose of about 30 mg/kg body weight which was given as an intravenous injection through an aural vein Complementary injections of Nembutal® were given until the Achilles reflex was no longer present The animal was strapped in the supine position on to a special sled formed operation table with the hip and knee joints flexed at 60 The hind limbs were supported under the thigh the knee joint and the heel while the lower leg was free The leg was fixed to the operation table by straps over the thigh and foot In order to avoid traumatization of the lower leg no pressure was exerted against it during the operation After washing of the skin with spirit a 2 cm long arciform skin incision was made lateral to the knee joint A skin flap with its base on the medial side was dissected free and folded over medially The patellar ligament was exposed and incised longitudinally An awl which had been ground so as to produce four sides was then inserted into the medullary cavity under the patellar ligament so as to produce a hole about 4 5 mm in diameter and slowly and carefully rotated about 1 cm into the cavity

The contents of the medullary cavity were removed by one of the following three methods

1 *Reaming* The narrowest reamer with a diameter of 2 52 mm was first inserted into the medullary cavity slowly and under rotation The reaming was then repeated with successively wider reamers until a layer of cortex of an estimated thickness of $^1/_4$ $^1/$ mm had been removed from the middle part of the bone The reaming was performed intermittently about a half minute of reaming being followed by a half minute interval

2 *Suction* The contents of the cavity were sucked out through a polyethylene catheter with an inner diameter of 1 5 mm The suction was repeated three times and between each suction an elastic metal spiral about 1 mm thick and with a curved end was inserted into the medullary cavity under rotation in order to mobilize bone marrow attached to the endosteum

3 *Brushing* The content of the medullary cavity was mobilized by means of a bottle brush 7 mm thick and 2 cm long attached to a wire shaft The brush was inserted into the medullary cavity as far as the distal metaphysis and then withdrawn The brushing was repeated twice

The skin incision was closed with silk sutures and the wound covered with Nobecutan®

Bone Labelling

In order to label the newly formed bone an intravenous or intraperitoneal injection of tetracycline (Dumocyclin® Dumex[1]) was given in a dose of

[1] Dumocyclin was kindly supplied by Dumex Ltd Denmark

Table 1 *Rabbits for morphological studies after reaming of the medullary cavity*

* indicates that the animal is reamed in both tibias

Obs time	Growing animals	Adult animals
2 hours	27*	
4 h	28*	—
8 h	32* 33*	—
1 day	40* 61	9*
2 d	38*	10*
3 d	3 81 114 123 124 125	54 55 63 109 110
4 d	37* 41*	—
7 d	64 66 95 104 105 106	112 121 126
10 d	4	—
2 weeks	6 42* 45* 59 101 108 211 220 281 285	57 58 86 87 119
3 w	5 46* 47*	—
4 w	7 15* 51 52 96 97 216	75 88 89 100 113
5 w	13* 31*	73
6 w	30* 36*	—
7 w	—	11* 23*
8 w	14* 50 65 92 111	21* 67 77 83 84 85
10 w	—	39*
12 w	—	43* 56 69 70 76

The rabbits were kept separately in ordinary rabbit cages with floors of wire netting They were given free access to water and to food pellets with a standardized content of calories minerals and vitamins

Reamer Equipment for Widening of the Medullary Cavity

For reaming of the medullary cavity plain excavating burrs for dental use manufactured by Hager and Meisinger, Dusseldorf were used Eleven different burr numbers were used with burr head diameters of 2 52–4 72 mm The increase of the burr head diameter between each burr number was 0 1–0 3 mm A 15–20 cm long shaft in the form of a wire spiral was constructed of piano wire The external diameter of the wire spiral was 2 5 mm for the narrowest burrs and 3 5 mm for the widest

The burr was divided 10 mm below the head and the neck of the burr was ground down to a diameter of 1 mm The ground burr neck was inserted into the central canal of the wire spiral to about 2 mm from the head and soldered into the canal (Fig 1) The reamers so produced were kept standing in spirit when not in use For reaming of the medullary cavity the reamer shaft was fixed in a sterilized chuck which was driven by a flexible drive axle covered by a sterile linen bag and this axle was coupled to an electric motor with a rotation rate of 300 r p m The motor was controlled by a foot switch

the abdomen was opened by a midline incision The small blood vessels in the abdominal wall which had been severed at the laparotomy were left open The aorta was exposed below the renal arteries and ligated proximally Through an incision in the aorta a polyethylene catheter with an inner diameter of 1 1 mm was inserted distally until its tip lay immediately above the aortic bifurcation A strong blood flow was obtained through the catheter The catheter was connected to a drip infusion apparatus for infusion of the Indian ink solution The infusion pressure was about 130 cm H O As a rule the animals died when 200–300 ml of the solution had been infused Towards the end of the infusion the infusion rate decreased spontaneously and gradually After infusion of 800–1000 ml the infusion was discontinued Both legs were then exarticulated at the hip joint The skin was removed from the thigh and lower leg after which the limb was fixed in 10 neutralized formalin solution contained in a large vessel After 2 days the tibia was dissected free from the skin and outer soft tissue Fixation in formalin was then continued for a further 5 days after which the preparations were frozen to −20°C

Macroradiography

Macroradiographs were taken of both tibias in the frontal projection

Preparation

In the general morphological series the tibia in the deep-frozen state was divided with a saw 2 5 and 7 5 cm from the tibiotalar joint The intermediate 5 cm of the diaphysis was used for the preparation of sections for fluorescence microscopy microangiography and conventional histology From each end of the diaphyseal preparation ¹/. cm was sawn off and decalcified A further ¹/ cm was sawn off from each end and embedded in methyl metacrylate The remaining 3 cm long part of the diaphysis was sawn longitudinally into one fibular and one tibial half The fibular half was decalcified and embedded in paraffin The tibial half was embedded in methyl metacrylate In the other series of experiments the tibia was divided according to some different scheme as described in the relevant chapters

The preparations intended for plastic embedding were dehydrated in absolute alcohol which was changed daily for 5 days They were then transferred to non polymerized methyl metacrylate in which they were kept for 4 days after which they were embedded in glass tubes in partially polymerized methyl metacrylate which was finally polymerized in a heat chamber at 30 C during a period of 3–4 days Slices ¹/ mm thick were then sawn



Fig 1 The reamer with its flexible axis is inserted through the patellar ligament which was incised longitudinally

50 mg/kg body weight Animals studied at shorter observation times than 3 days did not undergo bone labelling All other animals were given the labelling substance intraperitoneally 2 days before the angiographic examination This labelling was called labelling 2 In the main experimental groups all animals were given one further labelling called labelling 1 intravenously or intraperitoneally 0–7 days after the reaming of the medullary cavity As a rule for labelling 1 the growing animals were given tetracycline 0–1 day after the operation and the adult animals 1–4 days after the operation The remaining animals not belonging to the main experimental groups with an observation time of >3 days underwent labelling 1 at varying times after the operation

Microangiographic Procedure

200 ml of Pelikan Indian ink suspended in 800 ml of physiological saline was used as the infusion medium At the end of the observation time the animal was anaesthetized with Nembutal® and 2 ml of heparin (5000 U ml) was given intravenously The animal was placed in the supine position and

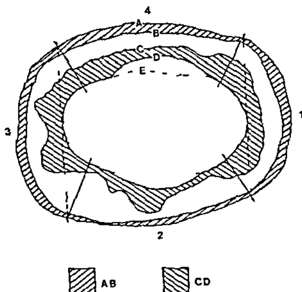


Fig 2 Drawn image of the distal fluorescence section with the vascular front drawn in The drawing is divided into 4 sectors 1 tibial 2 dorsal 3 fibular 4 ventral
Line *A* The outer boundary of the outer fluorescent line resulting from labelling 2
Line *B* The inner boundary of the inner fluorescent line resulting from labelling 1
Line *C* The vascular front obtained from the Spalteholz preparation
Line *D* The peripheral boundary of the bone removed on reaming
Line *E* The inner borderline of the orginal cortex against the medullary cavity
When no bone was removed on reaming lines *D* and *F* coincide
Each sector is divided into the following areas
AB Bone formed betwe n and during labellings 1 and 2
BF Original cortex
BC Vascularized part of original cortex
CD Avascular part of original cortex
DE Part of original cortex removed on reaming

(line *A* see below) lay on the fibular side of both tibial corners of the profile drawing A line was drawn parallel with this line through the fibular boundary of the medullary cavity The fibular corners then lay within the fibular sector From the respective intersection points with the outer fluore scence line lines were then drawn straight through the cortex to the me dullary cavity These lines coincided essentially with the principal direction of the intracortical vessels

B Assessment of Vascularization

On the plastic embedded non-decalcified cross sections which had been photographed the Indian ink filling of the intracortical vessels could only be assessed incompletely For this purpose thi ker preparations treated ac cording to the Spalteholz technique were required From the plastic-embed ded preparations a further $^1/_2$ mm thick section was therefore cut

from the methyl metacrylate-embedded specimens, parallel with the cut surface of the bone For this purpose a bandsaw was used with a 100 μ set blade, whereby a distance of 300 μ was obtained between the preparations The slices were ground and polished by hand with sandpaper to a thickness of 50–100 μ and then mounted in Permount under a cover glass Fluorescence microscopy was performed with a conventional binocular microscope with Zeiss large fluorescence equipment Selected fluorescence preparations and Spalteholz preparations were photographed on Echtachrome High Speed 23 din for daylight, Kodachrome II or Addox kb 14

The bone preparations intended for preparation of Spalteholz specimens and conventional histological specimens were decalcified with 5 % nitric acid and embedded in paraffin From the paraffin embedded preparations $^1/_2$ mm thick sections were sawn parallel with the cut surface of the bone The paraffin was removed with xylol the sections treated according to the Spalteholz technique, and studied in a binocular microscope

In order to assess the amount of newly formed bone, the amount of bone removed on reaming and the degree of intracortical vascular damage the following methods were used

A Division of Preparations

Colour diapositives of transverse plastic embedded cross sections were projected in a magnification apparatus and the images drawn on paper, so that the total longitudinal magnification was 30 1 times The images from the treated side and from the control side were always projected in such a way that equivalent images were obtained (Fig 2) On the profile drawing the outer boundary of the outer fluorescence line the inner boundary of the inner fluorescence line and the borderline between the medullary cavity and the cortex were drawn in On the profile drawing from the treated side the points at which the reamer had cut into the cortex were marked on the latter borderline The central borderline for the bone which had been removed during the reaming was determined by comparison with the corresponding area from the control side as follows The diapositive from the control side was projected on to the profile drawing from the treated side so that the corresponding endosteal line of the control side passed through the points in the drawing of the treated side at which the reamer had cut into the cortex The intermediate endosteal borderline of the control side was then drawn on the profile drawing of the treated side

The profile drawing was divided into four sectors (1) tibial (2) dorsal (3) fibular and (4) ventral The boundaries between the sectors were determined by drawing a line through the tibial boundary of the medullary cavity so that the intersection between this line and the outer fluorescence line

3 *Area CD* The part where the vessels were not filled with Indian ink (avascular part of original cortex)

4 *Area DE* The part wich had been removed on reaming of the medullary cavity (part of original cortex removed on reaming)

The size of the different areas was usually determined planimetrically and expressed in per cent of the whole cortical area at the start of the experiment the original cortex i e of the area *BE* (see below)

C Special Methods of Measurement

In the following cases the position of line *A* could not be determined exactly on profile drawing of the colour diapositive of the fluorescence preparation

1 When there was no periosteal new bone formation at the second tetracycline labelling In these cases the borderline between periosteum and underlying bone could sometimes not be identified

2 When the bone formation was very rapid at the second labelling especially on the formation of trabecular bone The borderline between fluorescence labelled bone and later formed non labelled bone was then often diffuse and could not be determined exactly

The position of line *B* on the projected image was uncertain in the following cases

1 When labelling 1 gave weak fluorescence The fluorescence line which then occurred could then be impossible to identify on the projected image

2 When at the first labelling the bone grew rapidly with the formation of primary osteones In these cases the fluore cence from the maturing osteones central to the labelling line B could completely obscure this line

The technical error in drawing of the projected image could also be of great importance for the reliability of the recording if the distance between lines *A* and *B* on the profile drawing was very small and only amounted to about one mm

If the preparation was sawn obliquely the fluorescence lines would appear broader than they were in reality If for example the preparation was sawn at an angle of 10 and was 50 μ thick the distance *AB* would be lengthened by 8 8 μ This would mean that the value obtained for the bone area *AB* would be approximately 0 1 too large calculated in per cent of the area *BE* If for example area *AB* comprised 0 5° of area *BE* the value obtained for area *AB* would be 0 6 %

In order to avoid the above difficulties direct measurements were also made on fluorescence preparations in the microscope for recording of the

adjacent to the section which was used for preparing the photographed fluorescence section The methyl metacrylate was removed with chloroform after which the section was decalcified and treated according to the Spalteholz technique By means of a microscope and a table which could be raised or lowered, the image of this Spalteholz preparation was given the same size as and projected onto the drawn image of the corresponding fluorescence preparation The vascular pattern in the projected image of the Spalteholz preparation comprised a summation image of the vessels in the $^1/_2$ mm thick section The borderline between the intracortical vessels which had filled with Indian ink and those which lacked Indian ink was called the vascular front This line was drawn between that part of every Indian ink-filled vessel which lay nearest to the medullary cavity In cases where no Indian ink-filled vessels were found within a distance of 3–4 mm the borderline was drawn towards the periphery until an Indian ink filled vessel was seen within this distance No Indian ink-filled vessels were then found in the cortex central to the vascular front, but peripheral to this borderline some Haversian canals without Indian ink-filled vessels could be seen

The distance between the plastic embedded preparation and the corresponding Spalteholz preparation was about $^1/_2$ mm, and the profile drawing obtained thus comprised a summation image of one fluorescence preparation and one Spalteholz preparation taken about $^1/_2$ mm from one another

When the vascular front had been drawn, the following lines were then present on the profile drawing counting from the periphery (see Fig 2) *A* the outer boundary of the outer fluorescence line This fluorescence line resulted from tetracycline labelling 2 which was given 2 days before the angiographic examination *B* the inner boundary of the inner fluorescence line This fluorescence line resulted from labelling 1 *C* the vascular front obtained from the Spalteholz preparation *D* the peripheral boundary for the bone removed on reaming *E* the inner borderline of the cortex against the medullary cavity and the inner boundary of the bone removed on reaming In the unreamed areas of the cortex, lines *D* and *E* coincided See fig 2

The profile drawing of the cortex was thus divided into the following areas within each sector

1 *Area AB* The part of the cortical cross section area which was labelled by the two tetracycline injections and the part between these labelling lines

2 *Area BC* The area of original cortex in which the vessels were filled with Indian ink on angiography (vascularized part of original cortex)

3 *Area CD* The part where the vessels were not filled with Indian ink (avascular part of original cortex)

4 *Area DE* The part wich had been removed on reaming of the medullary cavity (part of original cortex removed on reaming)

The size of the different areas was usually determined planimetrically and expressed in per cent of the whole cortical area at the start of the experiment the original cortex i e of the area *BE* (see below)

C *Special Methods of Measurement*

In the following cases the position of line *A* could not be determined exactly on profile drawing of the colour diapositive of the fluorescence preparation

1 When there was no periosteal new bone formation at the second tetracycline labelling In these cases the borderline between periosteum and underlying bone could sometimes not be identified

2 When the bone formation was very rapid at the second labelling especially on the formation of trabecular bone The borderline between fluorescence labelled bone and later formed non labelled bone was then often diffuse and could not be determined exactly

The position of line *B* on the projected image was uncertain in the following cases

1 When labelling 1 gave weak fluorescence The fluorescence line which then occurred could then be impossible to identify on the projected image

2 When at the first labelling the bone grew rapidly with the formation of primary osteones In these cases the fluore cence from the maturing osteones central to the labelling line B could completely obscure this line

The technical error in drawing of the projected image could also be of great importance for the reliability of the recording if the distance between lines *A* and *B* on the profile drawing was very small and only amounted to about one mm

If the preparation was sawn obliquely the fluorescence lines would appear broader than they were in reality If for example the *preparation* was sawn at an angle of 10 and was 50 μ thick the distance *AB* would be lengthened by 8 8 μ This would mean that the value obtained for the bone area *AB* would be approximately 0 1 % too large calculated in per cent of the area *BE* If for example area *AB* comprised 0 5% of area *BE* the value obtained for area *AB* would be 0 6 %

In order to avoid the above difficulties direct measurements were also made on fluorescence preparations in the microscope for recording of the

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The profile drawing of the cortex was thus divided into the following areas within each sector

1 *Area AB* The part of the cortical cross section area which was labelled by the two tetracycline injections *and the part between these labelling* lines

2 *Area BC* The area of original cortex in which the vessels were filled with Indian ink on angiography (vascularized part of original cortex)

sectional area of 7 4 % (S E ± 0 64) was removed on reaming (In growing animals 6 6° and in adult animals 8 4°)

Tetracycline Labelling of Newly Formed Bone

Tetracycline was used for labelling of the newly formed bone since this is a simple method which in several investigations has given almost perfect correlation with microroentgen and autoradiography (Harris *et al* 1962) and also with histological studies of osteoid bands (Kelly *et al* 1965, Van derhoeft *et al* 1962) Tetracycline forms chelates with calcium ions When ever calcium ions are interchanged or set free i e during mineralization and demineralization an equilibrium reaction with tetracycline takes place (Eger *et al* 1967) Injected tetracycline becomes bound to all cartilage and bone which is undergoing mineralization (Frost *et al* 1961 Vanderhoeft *et al* 1962) The level of tetracycline in the blood is adequate to label the bone for approximately 8 hours following an intraperitonal injection (Tapp 1966) Tetracycline given by this route can be expected to give the same good labelling as that injected intravenously (Ahlgren 1968) The diffuse tetracycline fluorescence in the tissues disappears within 2 days after the injection (Harris *et al* 1962 Frost *et al* 1961) and in order to avoid this source of error labelling 2 was given 2 days before the angiographic examination

Labelling of Howship s lacunae which was recorded by Hulth & Olerud (1962) takes place according to Eger *et al* (1967) during the resorption phase of the bone This labelling occurred often in the preparations of the present study The labelling band on bone resorption can be distinguished from that on bone formation by its thinness and by the fact that in the former case the border of the bone surface is uneven The binding of tetra cycline in the calcification zone—if the animal has not been given tetracyc line during the last day before death—has been described by Frost *et al* (1961) and Harris *et al* (1962) as a form of surface stain According to Hansson (1967) this tetracycline deposition occurs mainly postvitally *inter alia* in the fixation bath This labelling was sometimes observed in the present study as an extremely thin fluorescent band on the surface of the bone outside the fluorescent band from labelling 1 or 2 if the latter band lay at a short distance from the bone surface Since the labelling band in the calcification zone is always very thin it can usually be identified easily

The Bone suppressing Effect of Tetracycline

According to Eger *et al* (1967) tetracycline causes hypoplasia of dental enamel by (1) suppressing the formation of crystal nuclei (2) preventing

positions of lines A and B The measurements were performed at a magnification of 320 times The microscope could then be focused exactly to the upper layer of the preparation, which eliminated essentially the increase in breadth which occurred if the preparation was sawn obliquely The exact positions of lines A and B could also be more easily established even if the labellings were weak or if irrelevant fluorescence disturbed the image

Approximation of area AB was performed as follows On the profile drawing line A was divided in each sector into six equal parts by means of dividers The division points were denoted points 0, 1, 2 3 4, 5 and 6 The length of each sixth was recorded on the profile and denoted a On the preparation the distance between lines A and B included the width of the two fluorescent bands, was measured with an ocular micrometer at *points 1, 3 and 5 and the mean value of these measurements* was given as the thickness (T) of the newly formed bone With the magnification used one ocular micrometer unit U corresponded to 3 5 μ Area AB was expressed in the same planimeter unit as was used in the planimetric determination of the other areas on the profile drawing of the fluorescence preparation The values for area AB so obtained were expressed in per cent of area BE

For approximation of area AB the following formula was used for each sector

$$\frac{T\ 3\ 5}{1000}\ 30\ 1\ 6a\ \frac{10\ 82}{10\ 000}\ \text{units}$$

where

$\frac{T\ 3\ 5}{1000}$ = the mean value of the three thicknesses of AB measured in the microscope at points 1 3 and 5 expressed i mm

a = $\frac{1}{6}$ of the length of line A within the sector expressed in mm

30 1 = the longitudinal enlargement of the fluorescence profile drawing obtained as the mean value of 10 control measurements with s E = $\pm$0 05

$\frac{10\ 82}{10\ 000}$ = the number of planimeter *units corresponding to 1 mm*^{2}

Discussion of the Methods

The flexible shaft of the reamer made it possible for the reamer to follow the S shaped tendency of the medullary cavity In the tibial diaphysis especially in the distal part the medullary cavity is oval The reamer thus removed bone practically solely from the ventral and dorsal sectors, while only small amounts of bone were removed in the tibial and fibular sectors

From the area of the tibia from which the distal fluorescence section was taken 3 0–3 5 cm above the tibio talar joint a mean cortical cross

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water while about 200 ml of Indian ink was infused The animal usually died after infusion of this amount of Indian ink The flow through the small abdominal wall vessels was then profuse In two animals the bleeding vessels in the abdominal wall were ligated The venous pressure then rose during the infusion to about 40 cm of water Subsequently bleeding occurred from the omentum among other places after which the venous pressure gradually decreased No venous pressure exceeding 23 cm of water was recorded during the infusion when the abdominal wall vessels were left open

The profuse blood flow obtained from the catheter which had been inserted into the distal part of the aorta showed that the lower extremities are supplied with blood even if the aorta is ligated During the infusion the Indian ink was therefore mixed in successively higher concentrations with the blood which perfused the legs right up to the time when the animal died This method of perfusion has been found to give good visualization of the entire vascular system of the diaphysis including intracortical capillaries and sinusoids in the medullary cavity The vessels leading from the periosteum into the cortex are very narrow throughout however and there is a risk that these vessels may be obliterated by the Indian ink with the result that the filling of vessels in the underlying cortex will be incomplete In order to counteract the deposition of fibrin on the ink parti les the animals were heparinized Studies of longitudinal sections of Spalteholz preparations have also shown that within a height difference of a few mm large differences in Indian ink filling of the intracortical vessels seldom occur The vascular pattern in the Spalteholz preparation taken about 1/ mm from the fluorescence preparation can therefore be considered to reflect satisfactorily the Indian ink filling in the cortex of the fluorescence preparation

In the Spalteholz preparations which were prepared from paraffin-embedd d sections the soft tissue structures and cortex were well preserved These preparations make possible detailed studies of soft tissue vessels and intracortical vessels The Spalteholz preparations prepared from the primary plastic embedded bone swelled when the methyl metacrylate was dissolved with chloroform as a result of which the soft tissues around the bone and in the medullary cavity were destroyed Bone preparations often buckle but as a rule the cortex remains otherwise intact These preparations are therefore only suitable for evaluation of the intracortical vascular filling and not for evaluation of the vessels of soft tissues

Errors of Calculation

The error on calculating the area *CD* i e that area of the cortical cross section in which the vessels did *not fill* with Indian ink at angiography

the growth of crystallites, and (3) blocking the conversion by hydrolysis of primary octacalcium orthophosphate into apatite

Saxen (1966) found in *in vitro* studies that tetracycline in a concentration of 500 μg/ml completely inhibited the development of the calcified zone in bone rudiment The effect was irreversible after it had been present for 5 days Hansson (1967) found that tetracycline in a dose of 25 mg/kg body weight disturbed both the endochondral calcification process and the resorption of the cells of the degenerated cartilage

Tetracycline in the dose used here approximately 50 mg/kg can thus probably have a negative influence on the mineralization and growth of bone tissue Whether tetracycline also interferes with resorption of bone tissue is unknown The effect is greater at higher tissue concentrations (Hansson 1967)

In this material, on evaluation of the amount of newly formed bone the treated side was compared with the control side The rate of periosteal bone formation was at least at first, higher on the treated than on the control side A negative effect of tetracycline on bone mineralization and bone formation should therefore tend to reduce the difference between the treated tibia and the control tibia and thus not result in overestimation of the differences obtained

Absence of Bone Labelling

Six of the animals nos 46, 50 92 85, 77 and 56 showed a complete absence of fluorescent bone after labelling 2 All of these animals were given tetracycline in an intraperitoneal injection at the second labelling The reason for the lack of fluorescence is not clear but it might be that the tetracycline was injected into the large intestine and was therefore not absorbed These animals could not be evaluated completely on fluorescence microscopy Labelling 1 resulted in fluorescence of bone in all cases

Angiographic Technique

At the angiographic procedure the cut vessels in the abdominal wall were left open in order to counteract an increase of the central venous pressure and thereby reduce the risk of extravasation of Indian ink which easily occurs especially in the medullary cavity In order to obtain an idea of what pressure occurred in the venous system the central venous pressure was recorded in seven animals on a graded tube during infusion of Indian ink A polyethylene cather was introduced into the vena cava via the renal vein At the start of the infusion practically no measurable venous pressure was recorded When the vessels in the abdominal wall were left open after the laparotomy the venous pressure rose slowly to 15–20 cm

water while about 200 ml of Indian ink was infused The animal usually died after infusion of this amount of Indian ink The flow through the small abdominal wall vessels was then profuse In two animals the bleeding vessels in the abdominal wall were ligated The venous pressure then rose during the infusion to about 40 cm of water Subsequently bleeding occurred from the omentum among other places after which the venous pressure gradually decreased No venous pressure exceeding 23 cm of water was recorded during the infusion when the abdominal wall vessels were left open

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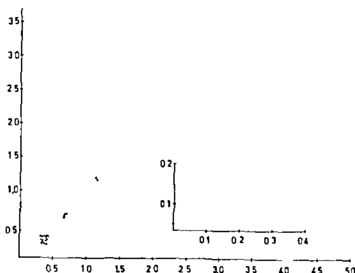


Fig 3 Relationship between the size of the area *AB* within each sector measured planimetrically on a drawn image (se p 29) (abscissa) and approximated according to the formula given on p 32 (ordinate) All sectors with approximated *AB* values greater than 0 2 U are included Of sectors with *AB* values below 0 2 U a representative number are included The figure shows that there is good correlation between the two methods of recording at approximated *AB* values greater than 0 2 U but a low correlation at lower *AB* values

was determined by drawing the same preparation, from animal 125, on five different occasions The mean value for area *CD* amounted to 50 5 % with S E = ±0 32 The reliability of the recording was considered to be adequate

On measurement of area *AB* the primary aim was to use planimetry as was used in the measurement of the other areas on the profile drawing It was found however that on measurement of small area the error in the drawing could be very large often several hundred per cent Area *AB* was therefore always approximated with the previously given formula (p 32) The error in this approximation was studied by correlating the results obtained on approximation of the area with the formula and the results obtained on planimetry (see Fig 3) With large *AB* values the correlation between the two methods was very high but with small *AB* values where approximation should give the most reliable value the correlation was low Approximation with the formula should thus be a better method in these cases than planimetry

Measurement of the thickness of *AB* in the microscope was performed at three points within each sector The change of the thickness within one sector usually takes place continuously and three measurements within each sector were considered to be representative of the sector

In order to determine the size of the error of measurement for the thick

Table 2 *Mean ıalue and standard deıiatıon for 10 measurements of the thıck ness of AB ın each of 5 sectors with trabecular bone primary osteones and cırcumferentıal lamellae*

	Trabecular bone					Primary osteones					Circumferential lamella[e]				
[Ani]mal no	125	45	45	45	281	125	281	244	240	237	51	58	123	2?0	9
[Me]an	32.5	117 4	72 6	123 4	95 4	7 8	32 6	7 1	22 8	38 6	23 1	8 8	3 2	11 1	2
	1 52	5 40	2 70	5 04	9 04	1 14	1 54	1 05	0 95	3 33	0 55	0 47	0 47	1 10	1

ness *AB* 10 separate measurements of the thickness were performed within each of five sectors with trabecular bone (*t*) primary osteones (*o*) and cir cumferential lamellae (*l*) (Table 2) For each series of 10 observations the mean value and standard deviation were calculated The size of the error of measurement for each individual bone structure was calculated with the aid of the standard deviations of the five individual series according to the formula

$$\sqrt{\frac{\sum \mathrm{SD}^2}{5}} = \mathrm{SD}_{t\ \ l}$$

The error of measurement ($\mathrm{SD}_{t\ \ l}$) of the individual observation was ±5 4 U for trabecular bone ±1 83 U for osteones and ±0 75 U for cir cumferential lamellae These errors comprise a reasonable estimate of the error to which the individual observation value for the respective bone structure is subject On measurement of the thickness *AB* the mean value of several determinations within one sector or within several different sec tors was calculated In these cases the error of the mean will be smaller than that of the individual observation

The variation caused by the systematic error of measurement can be correlated to the biological variation by forming the quotient

$$\frac{\sum \mathrm{SD}^2}{5} / \mathrm{SD}^2 m_{t\ \ l}$$

SD *m* is the variance for the mean value of the five observation series for trabecular bone primary osteones and circumferential lamellae respec tively and in this material is mainly an expression of the biological varia tion With the above formula the quotient for trabecular bone was 0 021 for osteones 0 017 and for circumferential lamellae 0 008 This is a rough measure of the relative importance of the error of measurement and the quotient is so low that the error of measurement can be regarded as of secondary importance in relation to the biological variations

The area of the bone removed on reaming was approximated from the profile drawing for the control side The error arising in this approximation was assessed by recording the natural difference between the right and left sides within the ventral and dorsal sectors in five control animals The endosteal line within the middle $^4/_6$ of the sectors from the profile image from the left tibia was drawn over the corresponding line on the profile image from the right tibia and the area between these lines was calculated and expressed in per cent of area *BE* The mean difference in the ventral sector was −0 4%, S D ±6 6 and in the dorsal sector 0 5%, S D ±2 7

Pressure Variations in the Medullary Cavity on Reaming and Brushing out of the Cavity in the Rabbit

Wehner (1968) has shown that on closed reaming and nailing of tibial fractures in man pressure variations from −100 mm Hg to +120 mm Hg can occur in the medullary cavity (See p 6) Larsen (1938) considers that an intramedullary pressure increase can give rise to necrosis of the cortex and Nick *et al* (1965) claim that the rise in pressure to about 75 mm Hg which can be observed in a fracture haematoma may be an important factor in fracture healing

Recording of the intramedullary pressure variations which occur in the medullary cavity on reaming and brushing by the method used in the present study was considered to be motivated here as an aid to establishing the cause of the intracortical vascular damage

Material

Two adult rabbits were used

Method

The anaesthesia and operative technique were as described on pages 25

The intramedullary pressure was recorded in the distal tibial metaphysis which was exposed ventrally about 1 ¹/ cm above the tibiotalar joint A hole 3 3 mm in diameter was drilled here through the ventral cortex The hole was plugged with a plastic plug through which a polyethylene catheter with an outer diameter of 1 5 mm and with a wall thickness of 0 2 mm was inserted The catheter was filled with heparin solution and was connected to a pressure transducer (Elema-Schonander EMT 490A) the nominal range of recording of which is *0-300 mm Hg The pressure was recorded* by means of a direct writing ink recorder (Mingograf 42B Elema Schonander Solna Sweden) The apparatus was calibrated between each recording and correction for drift was made

Pressure recording was performed during the following stages of the operative procedure

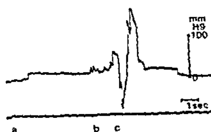


Fig 4

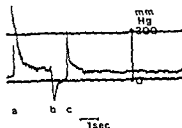


Fig 5

Fig 4 Recording of intramedullary pressure when the medullary cavity is opened with an awl under the ligamentum patellae At (*a*) the medullary cavity is opened carefully with the awl which is then held still in the hole At (*b*) the hole is widened carefully and at (c) the awl is forced down into the medullary cavity and rotated at the same time Pressure variations considerably exceeding 100 mm Hg can be seen

Fig 5 Recording of intramedullary pressure on insertion of a reamer into the medullary cavity At (*a*) the rapidly inserted rotating reamer comes into contact with endosteal bone At (*b*) the reamer is withdrawn a few cm and is then again forced into the medullary cavity (c) When the reamer is moved up and down in narrow parts of the medullary cavity considerable pressure variations can occur

1 When the medullary cavity was opened with an awl below the patellar ligament.
2 When the reamer was inserted in the medullary cavity
3 On reaming of the endosteal cortex in the medullary cavity
4 When the reamer was removed from the medullary cavity
5 When a bottle brush was inserted into and withdrawn from the medullary cavity

Results

The spontaneous pressure in the medullary cavity was found to be about 30 mm Hg

Recording at stage 1 When the medullary cavity was opened with an awl a fall in pressure was first noted When the awl was held still the pressure lay at a level of about 30 mm Hg On moving the awl again a further rise in pressure of the order of 25 mm Hg was obtained When the awl was forced down into the medullary cavity and rotated at the same time a pressure increase to considerably over 100 mm Hg occurred On movement of the awl considerable negative pressure was also observed (Fig 4)

Recording at stage 2 When the reamer was introduced under rotation into the medullary cavity a pressure rise was recorded When it was inserted slowly very small pressure increases occurred but when it was inserted quickly pressure increases to above 300 mm Hg were noted Large reamer heads appeared to cause greater pressure increases than smaller reamer heads under otherwise identical conditions (Fig 5)

Recording at stage 3 During the reaming a moderate and varying pressure rise of fairly long duration can be seen but rapid pressure variations of the

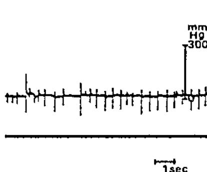


Fig 6

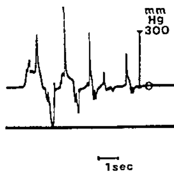


Fig 7

Fig 6 Recording of intramedullary pressure on reaming of the medullary cavity A moderate pressure increase of long duration and rapid pressure variations can be seen

Fig 7 Recording of intramedullary pressure on brushing in the medullary cavity Very large pressure variations can be seen

order of 200 mm Hg also occurred The rapid pressure variations were introduced by a negative phase and followed by a positive phase, the negative phase being the greater (Fig 6)

Recording at stage 4 When the reamer was withdrawn from the medullary cavity the pressure in the cavity decreased to below zero The order of magnitude of the decrease was dependent upon the rate at which the reamer was withdrawn Considerable negative pressures were recorded when the reamer was withdrawn rapidly (Fig 5)

Recording at stage 5 When a bottle brush was inserted into the medullary cavity a pressure increase to considerably over 300 mm Hg more than twice the range of the transducer was recorded When the brush was withdrawn there was a considerable decrease in pressure (Fig 7)

Discussion

When the medullary cavity is opened carefully with a rotating awl which is only inserted about 1 cm into the medullary cavity and the reamer is then introduced slowly and under rotation the pressure in the distal part of the medullary cavity does not increase to more than about 60 mm Hg which is twice the normal medullary cavity pressure It seems that under these circumstances the reamer head is able by a pump action to gradually transport backwards parts of the contents of the medullary cavity past the reamer head and thereby help to prevent the occurrence of a large pressure increase On reaming in endosteal bone large pressure variations can occur and variations up to 200 mm Hg were recorded These pressures are of the same order as those reported by Wehner (1968) The pressure variations give rise to varying pressures and a suction action in the Haver

sian canals of the diaphysis It is probable that on occurrence of these pressure variations material is easily squeezed into the Haversian canals from the medullary cavity The pressure variations in the medullary cavity can probably also cause the vessels in the Haversian canals which are very fragile to tear

Brushing of the medullary canal can give rise to even greater intramedullary pressure variations than reaming

Conclusions

Intramedullary pressure variations are probably an important cause of intracortical vascular damage on reaming of the medullary cavity The pressure variations can be reduced if the medullary cavity is opened carefully and if the reamer is moved up and down slowly in the medullary cavity

Determination of Temperature Increase on Reaming of the Medullary Cavity in the Rabbit

One possible reason for the occurrence of vascular trauma in the cortex on reaming of the medullary cavity may be that the reamer by friction heat can produce thermal damage Baar (1968) found that the function of the enzyme systems in human red blood cells was not affected negatively on heating if the temperature was kept below 42 C Lieber (1946) claimed that pain was induced from dentine if the temperature exceeded 55 C According to Hudoch *et al* (1939) irreversible changes occur in cell protoplasm at temperatures of 43 –44 C

In order to determine whether friction heat could give rise to thermal damage in the present material the temperature increase was recorded on reaming of the medullary cavity in the rabbit tibia

Material

Two rabbit tibias were used immediately after death of the animals

Method

The temperature was measured with a Thermocouple Applicator Type H 1 coupled to a Lab Thermocouple thermometer Type TE 3 with a measurement range of 0–50 C (Electrolab *Copenhagen*) *The Applicater Type H 1* measures with a thin measuring wire and has a setting time of 1-2 sec On recording a constant value was first obtained followed by a slow reduction The constant value has been given as the measurement value obtained

A water bath was heated to 38 C The thermoelement was placed in a stand 15 cm from the water bath and shielded from the bath In order to record the fall



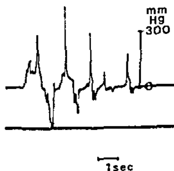


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(4) The pressure applied to the instrument Stronger pressures against the in strument give greater heat development

Brånemark (1958) ob erved a temperature increase of 10–12°C on grind ing of the cortex in rabbit fibulas at 300 r p m when no cooling fluids were used Vaughn & Peyton (1951) on drilling in dental enamel with drills 1 4–1 7 mm in diameter at 1300 r p m found a temperature increase of about 30°C Since the heat development in enamel has been estimated to be three times as great as in dentine (Peyton 1952) the heat development in dentine under these experimental conditions would have been about 10 C According to Branemark (1958) cortical bone is most closely comparable with dentine

In the present series of experiments on living rabbits reamers of relatively wide calibre were used The diameters of the reamer heads ranged from 3 02–4 92 mm the diameter increasing by up to 0 3 mm for each reamer number The reaming of the medullary cavity was performed successively the cavity being widened by a maximum of 0 3 mm with each reamer used and reaming of bone took place only by the most peripheral part of the reamer head Under these circumstances the heat development should be considerably less than if reamers of corresponding size were used in the reaming of solid bone in which case the whole of the anterior surface of the reamer would be in contact with the bone The rate of rotation used —300 r p m —is also relatively low The temperature increase observed in these erperiments thus corresponds well with previous experimnetal results

During operations in the medullary cavity in living animals the reamer is cooled by blood circulating in the cortex and by the blood which flows into the medullary cavity from the cortex With the method used for assessing the temperature increase on reaming the rise in temperature on reaming in living bone is probably not underestimated

Conclusions

Although the experimental conditions differ somewhat from those in ream ing of the medullary cavity in living animals it is reasonable to assume that about the same temperature increases max 3–4 C are produced locally in the medullary cavity in both cases

On intermittent reaming with no appre iable pressure against the reamer the temperature increase occurring should not damage the bone tissue

in temperature on the reamer head when this was transferred from the water bath to the thermoelement the head and about 3 mm of the shaft of reamer no 16 were held in the water bath for 1 min The reamer was then moved at a constant rate into contact with the measuring electrode This was done by inserting the measuring wire into one of the grooves of the reamer so that as large a contact surface as possible was created between the reamer and the measuring electrode The recording was re peated five times The same experiment was repeated six times with the water bath heated to 45–48 C

Freshly removed rabbit tibias were divided transversally in the middle of the diaphysis The distal part of the bone was fixed in the water bath which had been heated to 38 C so that the osteotomy surface lay a few mm above the surface of the water The head of reamer no 16 which is 3 9 mm in diameter was heated in the water bath for 1 min The medullary cavity of the tibia was then reamed for ½ min using slight pressure against the bone and with a rotation rate of 300 r p m after which the reamer was moved towards the thermoelement at the same rate as in the preparatory experiments and the temperature on the reamer head was recorded Five reaming experiments were performed The same reamer equipment was used as in the experimental series

Results

The mean reduction in temperature when the reamer was heated in the water bath and then transferred to the measuring electrode was 5°C (range 4–8°C) when the water bath temperature was 38°C At a water bath tem perature of 45–48°C the mean temperature reduction was 6°C with a range of 5–6°C

On reaming of the medullary cavity after preheating of the reamer the maximal increase in temperature was 3 C with a range from −2 to +3°C when correction was made for the temperature fall of 5°C noted when the reamer was transferred from the water bath to the thermoelement and 4°C when correction was made for a temperature fall of 6°C

Discussion

In these experiments the reamer lost heat via radiation fluid evaporation and conduction through the neck of the reamer to its shaft An attempt was made to keep these factors as constant and comparable as possible in the preparatory and main experiments

In odontology the development of heat on the drilling of teeth has att racted great interest Peyton (1952) found that the heat development on drilling is dependent upon (1) The material in which the drilling is per formed Drilling in enamel causes heat development three times as great as drilling in dentine (2) The type of instrument used Small drill heads give less heat development than large (3) The number of revolutions of the drill A low rate of rotation gives less heat development than higher rates

(4) The pressure applied to the instrument Stronger pressures against the instrument give greater heat development

Brånemark (1958) observed a temperature increase of 10–12°C on grinding of the cortex in rabbit fibulas at 300 r p m when no cooling fluids were used Vaughn & Peyton (1951) on drilling in dental enamel with drills 1 4–1 7 mm in diameter at 1300 r p m found a temperature increase of about 30 C Since the heat development in enamel has been estimated to be three times as great as in dentine (Peyton 1952) the heat development in dentine under these experimental conditions would have been about 10°C According to Branemark (1958) cortical bone is most closely comparable with dentine

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On intermittent reaming with no appreciable pressure against the reamer the temperature increase occurring should not damage the bone tissue

Effect of Reaming of the Medullary Cavity in the Rabbit Tibia

GENERAL REACTION OF THE ANIMALS

The animals bore weight on the treated leg on the day after the operation In no case was there any clinically manifest infection in the operation area and neither did any wound-rupture occur

MACRORADIOGRAPHIC STUDIES

On specimens observed at 0–2 weeks, thinning of the cortex on the treated side was often observed in the middle part of the tibia At an observation time of 2 weeks and later some animals showed a periosteal deposition of relatively low contrast density which was sometimes thicker than the original cortex The periosteal deposition occurred in some cases along the greater part of the cortex but in others it was localized to a limited area often located in the proximal fibular part of the diaphysis dorsal to the insertion of the fibula on the tibia In one preparation observed at 5 weeks *(13) (Fig 8) a zone of low density was observed at that location between* the original cortex and the periosteal callus tissue At the same time in some animals a patchy area of increased contrast density was seen in the medullary cavity In some animals studied at an observation time of more than 2 weeks there was considerably increased density in the medullary cavity and at the same time the borderline between the cortex and medullary cavity was indistinct

FLUORESCENCE MICROSCOPIC STUDIES

Normal Transverse Growth in the Diaphysis of the Long Bone in the Rabbit

The normal transverse growth of the long bone takes place in the diaphysis by the formation of lamellar bone on the periosteal surface at the same time as bone is resorbed from the endosteal surface The lamellar bone can consist of primary osteones or of circumferential lamellae When the rabbit is 3–4 months old its periosteum in the distal part of the diaphysis in the ventral sector often forms primary osteones so rapidly that several layers of osteones mature *simultaneously* In the dorsal sector the formation of la



Fig 8 X ray picture of rabbit tibia 5 weeks after reaming of the medullary cavity A zone of low density between the old cortex and a newly formed thin cortex on the dorsal side of the bone indicates a cavity in the callus Increased contrast density is seen in some areas in the medullary cavity (The same animal as in Fig 20)

mellar bone is as a rule alternated with bone resorption during this time In the tibial and fibular sectors lamellar bone is usually formed No woven bone was observed in this material during normal periosteal bone growth The rate of periosteal bone formation decreases during growth The previously formed primary osteones are superimposed during growth by circumferential lamellae

On the endosteal surface resorption alternates with the formation of lamellar bone

Parts of the cortex are reconstructed successively According to Owen *et al* (1955) this takes place especially in those areas of the cortex where in their opinion there are residual fragments of calcified epiphyseal cartilage On tetracycline labelling these areas of reconstruction appear on cross section as fluorescent ring shaped structures and on longitudinal section so-called cutter heads (Schenk 1963) can be observed during the formation of secondary osteones (Color pl 1 *a b* 3 *a)*

Fluorescence Microscopic Observations after Reaming of the Medullary Cavity

The material for this study comprised animals in Table 1 In the subperiosteal layer the morphology and reconstruction of the newly formed

bone were especially studied, and in the cortex the initial absence of bone formation and the rebuilding of vascularized and avascular cortex In the medullary cavity a study was made of the primary absence of fluorescence on endosteal bone, new bone formation bone resorption and restoration of the normal medullary structures

For the evaluations, each section was compared with the corresponding section from the control side in cases where only one tibia was treated (61/86 animals) The animal numbers are referred to table I D indicates the distal transverse section and P the proximal transverse section

Observation time 0–2 days

These animals were not given tetracycline Two of the animals (27 and 28) showed subperiosteal bleeding at the insertion of the fibula on the tibia

Observation time 3 days

Labelling 1 was given 1 day postoperatively

Periosteum The periosteum on the treated side had usually formed bone and osteoid tissue of the same structure as on the control side In some cases however woven bone had formed on the treated side while on the control side lamellar bone was observed

In the formation of woven bone beams or spicules of osteoid were first formed which later become calcified between two periosteal blood vessels Two closely adjacent beams were then united by bone, which formed a bridge over vessels lying nearby

The development of the periosteal bone formation could be followed by giving tetracycline at different time points after the operation and studying the location in the bone tissue at which the tetracyline was deposited When tetracycline was given at the time of the operation the fluorescent band always had the same appearance and thickness on the treated side as on the control side The structure of the bone and osteoid outside the fluorescent band showed however that woven bone could have been formed later than 8 hours postoperatively

When tetracycline in growing animals was given on the day after the operation, homogeneously fluorescent beams or spicules of woven bone up to 100 μ high were found between two blood vessels during the formation of trabecular bone (Fig 9) (125 D) In some preparations (125 P 124 P) incomplete fluorescent bridges between adjacent beams could be seen peripheral to the blood vessels When primary osteones were formed within an area where such osteones had been formed before the operation the post operatively formed primary osteones were often built of lamellar bone alone Beam shaped structures of woven bone sometimes occurred instead between



Fig 9 Distal fluorescence cross section of ventral cortex observation time 3 days Growing animal 125 labelled on day 1 Fluorescent spicules of newly formed subperiosteal bone are seen and between these radiating blood vessels The visib e part of the cortex is well vascularized from periosteal vessels

blood vessels in the same way as in the formation of trabecular bone This latter type of primary osteone developed even when circumferential lamellae had been formed before the operation or when preoperatively the periosteum had been inactive

In the adult animals many sectors showed no active bone formation but when bone formation did occur almost only circumferential lamellae were observed at 3 days

In a preparation from the growing animal 125 P a haemorrhage about 1 mm thick which had not taken up Indian ink was seen on the fibular side cranial to the insertion of the fibula on the tibia In the angle between the raised periosteum over this haemorrhage and the cortex newly formed trabecular bone was observed (Fig 10) The smooth bone surface under the centre of the haemorrhage completely lacked flourescence Minor haemorrhages in the corresponding region were seen in a further three growing animals (3 114 124) and two adults (54 110)

Cortex In the cortex signs of absence of bone formation activity were observed on the treated side Thus fluorescence was lacking in many areas adjacent to the medullary cavity and on the endosteal surface where fluorescent bone was present on the control side (Color pl 1) This absence of

bone were especially studied and in the cortex the initial absence of bone formation and the rebuilding of vascularized and avascular cortex In the medullary cavity a study was made of the primary absence of fluorescence on endosteal bone, new bone formation bone resorption and restoration of the normal medullary structures

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Fig 11 Proximal fluorescence cross section of fibular cortex observation time 3 days Growing animal 124 labelled on day 1 Indian ink filled blood vessels are traversing the cortex to the medullary cavity Extravasation of Indian ink is seen in the medullary cavity close to the endosteum Bone fragment in the medullary cavity adjacent to the Indian ink extravasation are fluorescent which is a si n that tetra cycline has diffused out into the medullary cavity blood clot here 1 day after the operation

the first and second labellings were often confluent In some of the youngest animals however two separate fluorescent bands were seen In these cases the outer band was broader than the inner (e g 64) This indicates that the rate of bone formation was higher 5 days than 1 day after the operation assuming that the absorption conditions of the tetracycline were the same on the two labelling occasions Since tetracycline was given as an intraperitoneal injection both at labelling 1 and 2 these conditions should have been identical

Primary osteones with woven and trabecular bone which had been labelled 2 days postoperatively showed in growing animals broader fluorescent beams between the blood vessels than tho e which were labelled on the day after the operation (Fig 12) Complete bridges were often observed over the blood vessels (65 97) From the labelling given 3 days after the operation (83) both broad beams between the blood vessels and bridges over them were fluorescent in both growing and adult animals A suggestion of fluorescence of beams leading to osteones of the next generation was



Fig 10 Proximal fluorescence cross section of fibular cortex observation time 3 days Growing animal 125 labelling on day 1 postoperatively There is a subperiosteal haematoma dorsally *and between the tibia and fibula The bone surface is inactive in* the central part under the haematoma but around this part even on the fibula trabecular bone *is formed*

bone formation was most clearly observed in the young animals in which normally there is active reconstruction of the inner part of the cortex In the cortical areas in which no bone formation activity was observed Indian ink filling of the intracortical blood vessels was also lacking

Medullary cavity In one preparation (124 P) an almost sector shaped area in the medullary cavity containing fluorescent bone fragment was found (Fig 11) These bone fragments had been detached from the endosteal cortex on reaming Passing to this area from the periosteum through the cortex was an Indian ink filled blood vessel and extravasation of Indian ink was observed in the medullary cavity blood clot between the fluorescent bone fragments and the endosteal surface In the remaining parts of the preparation the medullary cavity was filled with a clot containing non fluorescent bone fragments

Observation time 1 week

Labelling 1 was given 1 day and labelling 2 5 days postoperatively

Periosteum When lamellar bone had formed the fluorescent bands from



Fig 13 Distal fluorescence cross section of ventral cortex observation time 4 weeks Growing animal 7 labelled on days 7 and 26 postoperatively In the subperiosteally formed primary osteones ring shaped structures of lamellar bone show fluorescence after labelling 1 The osteones are almost closed at labelling 2 and are covered by circumferential lamellae In the inner part of the cortex reconstruction is taking place The bone trabeculae in the medullary cavity surrounded by wide Indian ink filled vessels are undergoing extensive resorption but deposition of bone is also observed

becular bone and primary osteones was observed at the insertion of the fibula on the tibia without any signs of resorption or reconstruction in this callus tissue In no animal was any major subperiosteal bleeding observed

Cortex In one animal (95) there was a tendency to widening of some bone canals in the subperiosteal part of the original cortex In the inner parts of the cortex an absence of fluorescence was observed in the same way as described for an observation time of 3 days

Medullary cavity The medullary cavity contained a blood clot containing bone fragments In several preparations newly formed blood vessels had invaded the medullary cavity Around these vessels a wreath of small fluorescent old bone fragments was seen but no newly formed bone was observed in the medullary cavity

Observation time 2 weeks

Labelling 1 was given 1 to 7 days and labelling 2 12 days postoperatively

Periosteum In one growing animal in which lamellar bone was formed during labelling on days 1 and 12 after the operation the fluorescent band



Fig 12 Proximal fluorescence cross section of the fibular part of the cortex observation time 8 weeks Growing animal 65 labelled 2 and 54 days postoperatively There are *trabeculae of woven* bone and bridges over vessels *fluorescence labelled 2 days* postoperatively Labelling 54 days postoperative y shows that the osteones were closed at that time The osteones are covered with circumferential lamellae after partial superficial resorption Reconstruction is taking place in the inner half of the cortex The *bone trabeculae in the visible part of the medullary cavity are resorbed and replaced* by almost *normal marrow*

also frequently ob erved When tetracycline had been given 4 days post operatively bridges to osteones of *the* second generation and beams to third generation osteones were sometimes fluorescent When tetracycline had been *given 7 days after the operation* the beams of woven *bone between* blood *vessels to primary osteones of the first generation were no longer fluores* cent *(Fig 13) In these* preparations fluorescence was *observed instead in* a ring shaped layer of lamellar bone around the blood vessels (7)

The woven bone which had been labelled 1 and 5 days after the operation showed however massive almost homogeneous fluorescence of all the newly formed bone (105)

In the adult animals the formation of circumferential lamellae predo *minated In* two animals (121 112) the formation of primary osteones was also seen *These* showed a *somewhat* lower degree of development than the primary osteones *in the young animals*

In several growing animals *(e g* 104 105) very *active formation of tra*

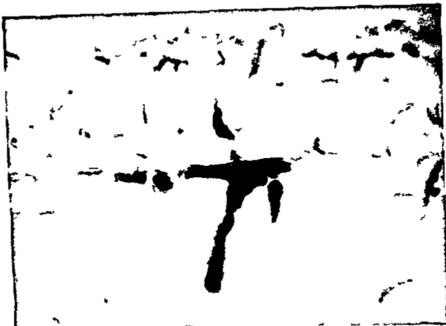


Fig 14 Proximal f uorescence cross section of fibular cortex observation time 2 weeks Adult animal 86 labelled on days 2 and 12 postoperatively Active periosteal callus formation with no appreciable resorption A canal in the subperiosteal original cortex is filled with an Indian ink filled vessel and is increasing in calibre which is e ident from its width and rough surface

cortex nearer to the medullary cavity many of the bone canals were con siderably wider than in the outer area of the cortex These canals ran through the cortex in the direction of the medullary cavity Their foremost part was often widened into a pear shape and comprised so called cutter heads (Fig 15) The bone surface was rough and partially labelled with a thin fluores ent layer of the type which can be seen on bone undergoing resorption Further peripherally on the walls of the bone canals new bone had been laid down whereby a secondary osteone had been formed In growing animals large resorption cavities occurred not infrequently in the inner part of the cortex In these cavities some preparations showed new formation of bone on the surface facing the medullary cavity In adult animals similar changes were een to those in the growing animals The resorption canals were narrower throughout however and no large resorption cavities were found in the cortex

Medullary cavity Blood vessels had invaded the medullary cavity in many of the growing animals and in some of the adults In no preparation was newly formed bone observed in the medullary cavity

after labelling 1 was narrower than that after labelling 2 In another growing animal which was labelled on days 7 and 12, the fluorescent band after labelling 1 was broader than that after labelling 2 The rate of bone formation thus appeared in the one case to be higher 12 days than 1 day postoperatively, and in the other case higher 7 days than 12 days postoperatively (59, 6) The tetracycline was given in the same way at both labellings in the respective animals

The newly formed, primary osteones and the trabecular bone had matured further From labelling 2 in first generation osteones ring shaped lamellar bone was fluorescent around blood vessels (Fig 14), and in second and third generation primary osteones and in trabecular bone beams of woven bone fluoresced between blood vessels The perivascular soft tissue had decreased correspondingly In many sectors resorption was in progress from the surface of the newly formed bone In the ventral and sometimes also the dorsal sector the bone formation often seemed to be greatest over that part of the cortex which had been most thinned by the reaming (Color pl 1 *b* Fig 18) Often in these cases primary osteones were formed in the area which was most thinned and circumferential lamellae at the sides of this area

In the region around the insertion of the fibula on the tibia no subperiosteal haemorrhage was observed in any of the preparations In many growing animals a large area of callus consisting of trabecular bone was found instead in this area Also in many adult animals trabecular bone was observed at this location but to a smaller extent than in the growing animals In the central parts of this callus an extensive resorption of the newly formed bone beams was in progress (Fig 16) In the peripheral parts of the callus new often lamellar bone was deposited on the bone bridges In this way the bone tissue became condensed peripherally and transformed successively to cortical bone (6) A similar reconstruction of callus was also observed in other areas of the diaphysis but only seemed to take place where a large amount of woven bone had been formed primarily and not when lamellar bone had been formed

Cortex In the outer parts of the cortex signs of reconstruction of the bone were observed in both growing and adult animals The bone canals for many of the blood vessels which passed from the periosteum into the cortex were thus wider on the treated side than on the control side in all growing animals and in two of the five adults The walls of the bone canals were often uneven due to the presence of Howship s lacunae which indicated bone resorption (Fig 14) In growing animals large resorption cavities occurred on the surface of the original cortex but only in areas over which trabecular bone had been deposited (45) (Color pl 2 *a*) In revascularized parts of the

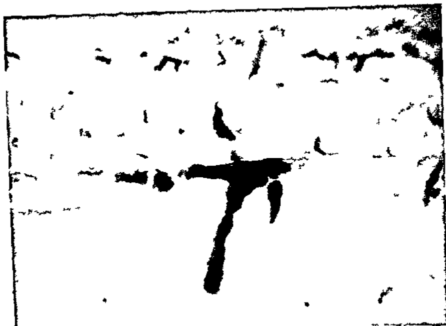


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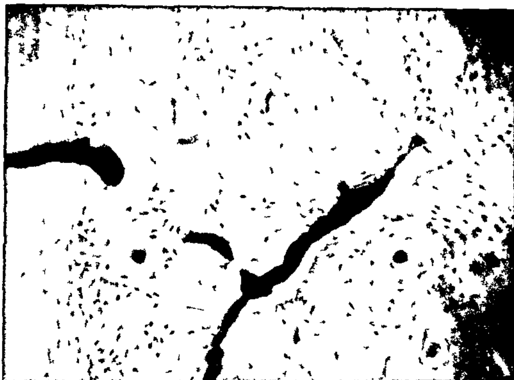


Fig 15 Distal fluorescence cross section of tibial part of cortex observation time 2 weeks Growing animal 108 labelled on days 1 and 12 postoperatively Revascularization of the cortex is taking place by means of cutter heads in the direction towards the medullary cavity (to the right) The cortex is being resorbed around the leading narrow vessel loop and new bone is being deposited on the wall of the eroded bone canal further peripherally close to fairly wide blood vessels massively filled with Indian ink

Observation time 3 weeks

Periosteum The blood vessel canals in the primary osteones formed post operatively had decreased further in width Active formation of lamellar bone was in progress on the walls of the bone canals around the blood vessels Extensive resorption was observed on the surface of the newly formed bone

Cortex In the cortex many of the bone canals had widened further and on the walls in many of the resorption cavities in the inner parts of the cortex fluorescent new bone was observed

Medullary cavity In several preparations from growing animals newly formed blood vessels and also a sparse amount of newly formed fluorescent woven bone was seen in the medullary cavity adjacent to the endosteum

Observation time 4 weeks

Labelling 1 was given 0–3 days and labelling 2 26 days postoperatively

Periosteum In the first generation primary osteones formed after the



Fig 16 Proximal fluorescence cross section of fibular cortex observation time 2 weeks Growing animal 6 labelled on days 7 and 12 postoperative y A large amount of trabecular bone has been formed in the dorsal angle between the fibula and ti bia The central part of the newly formed bone is undergoing resorption whi e the peripheral part is being condensed to cortical bone

operation the bone canals showed practically the same width as in the original cortex (Fig 13) The bone formation on the walls of these bone canals had almost ceased (7 97) The first formed primary o teones were in many cases superimposed by circumferential lamellae

In the area around the insertion of the fibula on the tibia a large amount of trabecular bone appeared to have formed primarily after the operation in two young animals At this observation time a hood of newly formed condensed periosteal bone was found in this area (Fig 17) Under this hood there was a cavity in the callus tissue filled with a tissue which on the fluorescence preparation resembled normal medullary tissue The cavity lay on the section right inside the callus tissue It was separated from the original cortex by a thin layer of bone which was partially undergoing resorption from inside the cavity On the largest part of the peripheral wall of the cavity active bone formation was ob erved (51 52) Only in prepara tions from one animal (97) was formation of woven bone under the periosteum in progress for the rest, only lamellar bone

Cortex In the young animals several bone canals in the outer part of the cortex were widened and filled with wide Indian ink filled blood vessels



Fig 17 Proximal fluorescence cross section of fibular cortex observation tim 4 weeks Growing animal 52 labelled on days 1 and 26 postoperatively There is a cavity in the periosteal callus tissue of trabecular bone The cavity is separated from the surface of the original cortex by a thin layer of bone which is largely undergoing resorption from the cavity on the peripheral surface of which bone formation is taking place

On the walls of these canals active bone reconstruction, with both resorption and bone formation was in progress Many bone canals in the outer part of the cortex did not seem to be undergoing any reconstruction however but showed the same appearance as on the control side In the inner parts of the cortex some of the growing animals showed large resorption cavities (Fig 19) which were partly lined with new fluorescent bone on the surface facing the medullary cavity while the opposite surface usually exhibited resorption In other parts of the inner cortex small cavities were seen often with bone formation around the entire circumference (Fig 13)

In the adult animals qualitatively the same reconstruction process was observed in the cortex as in the growing animals but the widened vascular canals were regularly considerably narrower and no large resorption cavities were found in the cortex

Medullary cavity In five of the seven growing animals and two of the five adults fluorescent bone trabeculae built of woven bone were found in the medullary cavity In some of the young animals and in one of the adults the central parts of the trabeculae were not fluorescent (Figs 13 18) This was observed especially in the trabeculae lying nearest to the endosteum

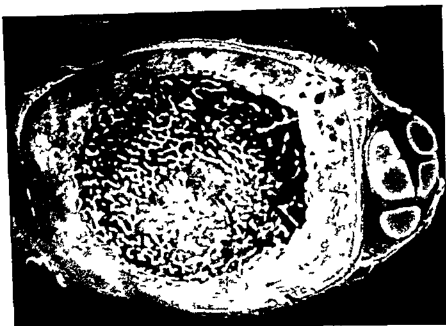


Fig 18 Distal fluorescence cross section observation time 4 weeks Growing animal 7 labelled on days 7 and 26 Almost completed periosteal new bone formation Extensive superficial resorption in the dorsal sector (below) Ventrally primary osteones were first formed and ventro-fibularly (above right) trabecular bone on which circumferential lamellae were deposited Reconstruction of the inner cortex is taking place especially in the fibular sector (right) In the centre of the medullary cavity there is a sparsely vascularized area with no newly formed bone trabeculae and peripheral to this area newly formed bone trabeculae with active bone formation are seen In the surrounding areas there are relatively few Indian ink filled vessels Adjacent to the endosteal cortex especially in the fibular and tibial areas bone trabeculae which are surrounded by wide vessels massively filled with Indian ink have been largely resorbed

The centre of these trabeculae had thus become mineralized earlier than 2 days before labelling 2 was given The trabeculae in the middle of the medullary cavity were often fluorescent on all surfaces but in some cases some surfaces lacked fluorescence often surfaces facing the periphery The nonfluorescent surface was then often uneven due to the presence of Howship s lacunae In three of the growing and three of the adult animals newly formed blood vessels of wide calibre usually with thin walls were observed in the medullary cavity adjacent to the endosteum

Observation time 5–6 weeks

Periosteum In one animal a large cavity was found in callus tissue in the area around the insertion of the fibula on the tibia (13) (Fig 20) From this cavity resorption of the underlying cortex was in progress



Fig 17 Proximal fluorescence cross section of fibular cortex observation tim 4 weeks Growing animal 52 labelled on days 1 and 26 postoperatively There is a cavity in the periosteal callus tissue of trabecular bone The cavity is separated from the surface of the original cortex by a thin layer of bone which is largely undergoing resorption from the cavity on the peripheral surface of which bone formation is taking place

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Fig 20 Proximal fluorescence cross section of fibular cortex observation time 5 weeks Growing animal 13 labelled on days 26 and 33 There is a cavity in the periosteal callus tissue of trabecular bone From the cavity which is filled with almost normal marrow tissue erosion is taking place of the underlying original cortex which in the centre under the cavity is avascular The same animal as in Fig 8

a fairly large cavity in the callus in the dorsal region (92) This cavity had a deeper location than in animals with shorter observation times (Fig 21) More than half of the cavity lay within the original cortex The surface of the cavity facing the medullary cavity showed a suggestion of fluorescence and on the other surface resorption of original cortex was in progress

Cortex In the growing animals the resorption processes in the cortex seemed to be less pronounced than at an observation time of 4 weeks and new bone formation predominated On the walls of most of the resorption canals and resorption cavities bone formation was observed In the inner parts of the cortex in growing animals large cavities were seen with only sporadic bone formation on the wall facing the medullary cavity In adult animals both resorption and new formation of bone were in progress on the walls of the resorption canals

Medullary cavity In all animals both growing and adult newly formed bone was found at some place in the medullary cavity In adult animals however the bone formation was often very sparse In the medullary cavity



Fig 19 Longitudinal fluorescence section observation time 4 weeks Growing animal 97 labelled on days 2 and 26 Some of the bone canals in the outer part of the cortex are widened and filled with rather wide vessels In the inner parts of the cortex large resorption cavities which are partly lined with new fluorescent bone can be seen

Observation time 8 weeks

Labelling 1 was given 0–4 days and labelling 2 54 days postoperatively

Periosteum The periosteum was inactive or had formed circumferential lamellae when labelling 2 was given The primary osteones which had formed previously in the postoperative course had usually become covered with a layer of circumferential lamellae (Fig 12) In some cases this had taken place after resorption of the peripheral parts of the woven bone which were fluorescent after the first labelling (65)

In the area of the insertion of the fibula on the tibia one animal showed



Fig 20 Proximal fluorescence cross section of fibular cortex observation time 5 weeks Growing animal 13 labelled on days 26 and 33 There is a cavity in the periosteal callus tissue of trabecular bone From the cavity which is filled with almost normal marrow tissue erosion is taking place of the underlying original cortex which in the centre under the cavity is avascular The same animal as in Fig 8

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Medullary cavity In all animals both growing and adult, newly formed bone was found at some place in the medullary cavity In adult animals however the bone formation was often very sparse In the medullary cavity



Fig 21 Proximal fluorescence cross section of fibular cortex observation time 8 weeks Growing animal 92 labelled on days 1 and 54 Condensed periosteal callus tissue which is undergoing resorption from the surface Between the callus tissue and the original cortex partly located in the original cortex there is a cavity whose central wall is undergoing resorption

in these animals large areas which had not become revascularized were seen In other areas there was revascularization by sparsely situated blood vessels without formation of new bone around the vessels In the growing animals resorption of bone predominated over new bone formation Many of the trabeculae observed at the border between the richly vascularized and the central sparsely vascularized areas lacked fluorescence even on the surface facing the centre The peripheral parts of the medullary cavity completely lacked trabeculae in many preparations In these areas the trabeculae had been resorbed and replaced by bone marrow which seemed on the fluorescence section to have a normal structure This bone marrow contained wide blood vessels usually veins On the endosteal surface especially within the reamed area a layer of newly formed lamellar bone was often found

Observation time 12 weeks

Labelling 1 was given 1–4 days and labelling 2 92 days postoperatively The group comprised only adult animals

Periosteum The fluorescence microscopic picture resembled that at an observation time of 8 weeks

Cortex In the outer parts of the cortex occasional blood vessel canals which were considerably widened were found On their walls bone formation was observed in some cases but as a rule there was no bone formation activity In the inner parts of the cortex resorption cavities were found the walls of which showed inactivity or bone formation but in fairly large areas of the cortex there were still no signs of reconstruction

Medullary cavity All the adult animals showed active bone formation in the medullary cavity but resorption of the trabeculae predominated in the peripheral areas of the medullary cavity Vessels of wide calibre usually veins but in some preparations also arteries were found in the medullary cavity The medullary cavity also contained areas with restored fat marrow of normal appearance in four of the five animals

Discussion

On reaming of the medullary cavity the medullary blood vessels in the diaphysis of the bone are completely destroyed at the same time as bone is removed from the endosteal surface of the cortex Reactive changes occur in the periosteum cortex and medullary cavity

Reaction of Periosteum

As in many previous investigations the periosteum in this study reacted with in reased bone formation The newly formed bone was of two morphological types lamellar bone and woven bone

Lamellar bone which can comprise circumferential lamellae or primary osteones is formed on normal periosteal growth in rabbits of the ages studied here and the formation of this bone could therefore be regarded as resumed or accelerated normal bone formation Frost (1963) pointed out that this bone when completely developed has maximum resistance to the physical loads on the skeleton This agrees with the present findings which showed that the central parts of the newly formed lamellar bone were not reconstructed during the period of maturation but appeared to have acquired their final properties at the initial stage

The causal mechanism for the formation of lamellar bone under the periosteum could not be elucidated by this material According to Frost (1963) the formation of lamellar bone is influenced by growth hormones thyroid hormones and space polarizing factors In the present study it was observed that the subperiosteal blood vessels were dilated during the time in whi h the periosteal bone formation was increased and during the subsequent phase when the bone resorption was potentiated The primary vascular dilatation may have been due to stasis in the blood vessels This can

lead to local anoxia and acidosis, which according to Richany *et al* (1965) and Johnson (1966) can induce subperiosteal bone formation According to Trueta (1963) dying or hypoxic osteocytes and endothelial cells influence the blood vessels, either by their action or by their inhibition, via vascular stimulating factors He considers that the bone formation can occur as a result of the vascular reaction

The formation of woven bone, which can consist either of primary osteones or trabecular bone results initially in a much more rapid increase in the thickness of the bone than the formation of lamellar bone and when trabecular bone is formed the cortical thickness can inrease twofold within the course of about 2 weeks In the normal growth of rabbits of the ages studied here, woven bone appears never to develop subperiosteally and its presence can be considered to be pathological so-called callus formation The formation of trabecular bone means that large amounts of woven bone have developed In this series trabecular bone was formed especially frequently within the area around the insertion of the fibula on the tibia In this area preparations studied at short observation times often showed subperiosteal haemorrhages which seemed to become resorbed within the course of about 1 week In preparations studied at longer observation times an abundance of woven bone which had probably been induced by such a haemorrhage was often observed at this site (see also p 118) The central parts of the trabecular bone were often reconstructed by resorption of the bone trabeculae and their replacement by normal medullary tissue whereby a cavity occurred in the callus tissue The callus tissue outside the cavity was reconstructed to cortical bone by the deposition of lamellar bone on the trabeculae around the blood vessels The callus cavity appeared to be formed at least partly inside the callus tissue and subsequently seemed to move in the direction of the medullary cavity by the deposition of bone on its peripheral wall simultaneous with resorption of its central wall The original cortex under the cavity was probably necrotic which may have been the reason that the callus cavity moved centrally Zucman *et al* (1968) demonstrated that a subperiosteal haemorrhage occurring after reaming of the medullary cavity consisted partly of squeezed out marrow fat which they found gave rise to abundant periosteal bone formation in which cavities could occur The woven bone thus seems to be a pathological bone formation which is often rebuilt during the process of maturation in order to adapt to the physiological demands placed on the extremity Frost (1963) considers that the formation of woven bone is governed by local stimulating factors and not by growth hormones thyroid hormones or space polarizing factors Neither is the structure of the collagen fibres adapted to the physical load on the skeleton according to Frost (1963) In the present material woven

bone was formed during the first 2–4 weeks after the operation but subsequently only lamellar bone was formed subperiosteally Charnley (1968) has pointed out that woven bone is a provisional bone which is resorbed when it becomes covered by lamellar bone In the woven bone the calcium crystals are less closely packed The bone is therefore permeable to tetracycline which then stains the entire bone tissue (Eger & Kammerer 1967)

On the surface of the newly formed periosteal bone alternating resorption and deposition of bone takes place after an observation time of about 2 weeks The newly formed woven bone is then covered with lamellar bone often when the surface of the woven bone has first been resorbed This alternation between superficial resorption and deposition of bone is according to Schenk (1967) the natural process of adaptation of the periosteum to different functional demands on the bone

Cartilage formation under the periosteum was not observed in any of the preparations of the present study This is in agreement with the findings of Bast *et al* (1925) and Richany *et al* (1965) They found cartilage formation from the periosteum only when the latter had been opened and never under intact periosteum

Reaction of Cortex

After reaming of the medullary cavity different areas of the cortex reacted in different ways depending among other things upon whether or not the blood circulation in the area remained undisturbed Growing and adult animals also reacted somewhat differently

Reconstruction of vascularized cortex

In those parts of the cortex where the circulation remained after the intramedullary reaming many of the intracortical bone canals began to increase in width during the first 1–2 weeks after the operation At an observation time of 4 weeks several of the widened canals had begun to decrease again in width by the deposition of bone on their walls Other canals continued to become wider on the other hand The increased circulation through the outer part of the cortex to its inner part and to the medullary cavity appeared in this way to be concentrated to a smaller and smaller number of blood vessels while the remaining vessels gradually became of decreased importance

Reconstruction of avascular cortex

The avascular areas of the cortex were revascularized from areas supplied with blood partly by means of cutter heads Schenk & Willenegger (1963)

lead to local anoxia and acidosis, which according to Richany *et al* (1965) and Johnson (1966) can induce subperiosteal bone formation According to Trueta (1963) dying or hypoxic osteocytes and endothelial cells influence the blood vessels either by their action or by their inhibition via vascular stimulating factors He considers that the bone formation can occur as a result of the vascular reaction

The formation of woven bone, which can consist either of primary osteones or trabecular bone, results initially in a much more rapid increase in the thickness of the bone than the formation of lamellar bone, and when trabecular bone is formed the cortical thickness can inrease twofold within the course of about 2 weeks In the normal growth of rabbits of the ages studied here woven bone appears never to develop subperiosteally and its presence can be considered to be pathological so called callus formation The formation of trabecular bone means that large amounts of woven bone have developed In this series trabecular bone was formed especially frequently within the area around the insertion of the fibula on the tibia In this area preparations studied at short observation times often showed subperiosteal haemorrhages which seemed to become resorbed within the course of about 1 week In preparations studied at longer observation times an abundance of woven bone which had probably been induced by such a haemorrhage was often observed at this site (see also p 118) The central parts of the trabecular bone were often reconstructed by resorption of the bone trabeculae and their replacement by normal medullary tissue, whereby a cavity occurred in the callus tissue The callus tissue outside the cavity was reconstructed to cortical bone by the deposition of lamellar bone on the trabeculae around the blood vessels The callus cavity appeared to be formed at least partly inside the callus tissue and subsequently seemed to move in the direction of the medullary cavity by the deposition of bone on its peripheral wall simultaneous with resorption of its central wall The original cortex under the cavity was probably necrotic which may have been the reason that the callus cavity moved centrally Zucman *et al* (1968) demonstrated that a subperiosteal haemorrhage occurring after reaming of the medullary cavity consisted partly of squeezed out marrow fat which they found gave rise to abundant periosteal bone formation in which cavities could occur The woven bone thus seems to be a pathological bone formation which is often rebuilt during the process of maturation in order to adapt to the physiological demands placed on the extremity Frost (1963) considers that the formation of woven bone is governed by local stimulating factors and not by growth hormones thyroid hormones or space polarizing factors Neither is the structure of the collagen fibres adapted to the physical load on the skeleton according to Frost (1963) In the present material woven

In the peripheral part of the medullary cavity in the growing animals of the present study at an observation time of 4 weeks resorption of the bone trabeculae facing the periphery of the bone often took place while bone formation still proceeded on the surface facing the parts of the medullary cavity which had not yet become revascularized At the same time new trabeculae were formed more centrally in the medullary cavity At an observation time of 8–12 weeks the trabeculae in the peripheral parts of the medullary cavity in the growing animals had often become completely resorbed and had been replaced by richly vascular medullary tissue The bone formation had then often partially ceased even on the trabeculae which lay in the centre of the medullary cavity on the border of areas which had not yet become vascularized or which were sparsely revascularized Branemark (1964) observed incipient resorption of the bone trabeculae after an observation time of 3 weeks and restored marrow tissue after 4 weeks Richany *et al* (1965) found that the marrow regeneration was largely accomplished 25 weeks after medullary removal

In the present material the adult animals showed considerably less bone formation in the medullary cavity than the growing animals Often at an observation time of 12 weeks large areas of the medullary cavity were still not revascularized In no preparation had the bone formation in the medullary cavity ceased 12 weeks after the operation

MICROANGIOGRAPHIC STUDIES

Normal Angiographic Pattern on Control Side

On Indian ink angiography with the method used here the entire vascular bed including intracortical capillaries and medullary cavity sinusoids was filled with the dye In the different vascular systems the vessels showed different degrees of Indian ink filling As a rule the periosteal vessels were massively homogeneously filled with the dye but the Indian ink columns in the vessels were sometimes interrupted by small unfilled or partially filled areas In the diaphyseal cortex parts of the capillaries were massively filled or lined with Indian ink Between these well filled parts short stretches of capillary which completely lacked contrast medium were seen *Arterioles* from the medullary cavity were as a rule massively filled and could often be followed to the middle of the diaphyseal cortex The cortex adjacent to the medullary cavity also showed however wide blood vessels in which the Indian ink lined the walls without filling the lumen The e vessels were often found to open in funnel shaped fashion into the intramedullary sinusoids The blood vessels in the subperiosteal bone were usually wider in the growing animals than in the adults

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described these cutter heads in fracture healing in the dog while Geiser (1963) claimed that they do not occur in the rabbit In the present study cutter heads were found to drill relatively narrow canals in the bone in an oblique direction towards the medullary cavity In addition to this form of revascularization of the cortex resorption cavities were formed in some cases in association with broom like vascular reactions In some growing animals very large cavities were formed There was a tendency for new bone to be formed on the peripheral surface of the cavity while at the same time resorption took place from its central surface In this way the cavity moved in the direction of the medullary cavity with increasing observation times An invasion of blood vessels and reconstruction of avascular bone was evident at an observation time of 2 weeks In growing animals the bone resorption in avascular cortex appeared to be most pronounced at an observation time of about 4 weeks, while the new bone formation seemed to be most active at about 8 weeks The rebuilding in the cortex thus took place when the periosteal bone formation activity had decreased This time course corresponds well with the findings of Andersson (1965) in the dog and of Richany *et al* (1965) in adult cats The small cavities in growing and adult animals appeared as a rule to close up completely This process took a long time however and at an observation time of 12 weeks many small cavities with active bone formation on the walls were observed Large cavities in the inner part of the cortex seem to have a tendency not to close completely In the present material at an observation time of 8 weeks cavities were found in the inner part of the cortex with no signs of either resorption or new bone formation on their walls Richany *et al* found large resorption cavities filled with normal bone marrow at an observation time of 4 weeks

Richany *et al* studied the development in adult cats over a long period and found that reconstruction in the cortex was essentially completed after 5 ¹/ months Trueta & Cavadias (1955) found that in adult rabbits necrotic areas were still to be seen in the cortex 8 months after disturbance of the endosteal circulation

Reaction of Medullary Cavity

Regeneration of the structures in the medullary cavity after scraping away of the bone marrow has been studied in detail histologically by Branemark (1964) and Richany *et al* (1965) The results obtained for the growing animals in the present study agree essentially with the findings of these authors Tetracycline labelling makes it possible to follow the formation and resorption of the bone trabeculae in the medullary cavity with greater reliability than do histological methods however

seen in some places In preparations observed at 24 hours (61) the periosteal blood vessels were wider on the treated than on the control side

Cortex At an observation time of less than 24 hours the filling of the intracortical capillaries was often difficult to evaluate since the Indian ink filled parts of one capillary were surrounded by long unfilled areas especially in the middle and inner part of the cortex At an observation time of 24 hours these unfilled areas had decreased greatly in number and length The vascular front (see p 30) could then be determined with more reliability

Under the subperiosteal haemorrhages the cortex usually showed no Indian ink filling of the blood vessels

Medullary cavity In all animals occasional blood vessels from the periosteum were seen to penetrate the entire cortex to the medullary cavity In the medullary cavity in front of the Indian ink filled vessel a minor extravasation of the dye was usually observed

Observation time 3 days

Periosteum It was a regular finding that the periosteal vessels were massively filled with Indian ink In four of the five young animals (3 114 124 125) and two of the five adults (54 110) there were subperiosteal haemorrhages localized to the area of the insertion of the fibula on the tibia (Fig 10) In no case was the haematoma infused with Indian ink In all young animals the periosteal blood vessels were wider and often more tortuous on the treated side than on the control side The same change was observed but much less pronounced in adult animals

Cortex From the periosteum Indian ink filled blood vessels penetrated into the cortex A tendency to a funnel shaped widening of these vessels nearest to the periosteum was noted on the treated side in all growing animals but was not observed in adult animals The dilatation of the blood vessels in the bone canals appeared to have taken place without the bone canals becoming wider at this time Under the subperiosteal haemorrhages the cortex showed a considerable lack of Indian ink filling of the blood vessels The filling of the intracortical vessels varied In the subperiosteal bone the blood vessels were often massively filled while those further inside the cortex often showed only grains of Indian ink along the walls In two of the five young animals (3 124) and one of the five adults (55) blood vessels filled with Indian ink were seen to run from the periosteum through the cortex to the medullary cavity

Medullary cavity In no preparation were any blood vessels filled with Indian ink found in the medullary cavity A minor extravasation of Indian ink was often observed just in front of the Indian ink filled blood vessels

In the medullary cavity both homogeneously filled, relatively narrow blood vessels, namely those which were seen to pass through half of the cortex and which were considered to be arterioles, and sinusoids the walls of which were *lined* with grains of Indian ink were found Small areas of medullary cavity sinusoids were completely empty of the dye The central vein of the medullary cavity was, as a rule lined with grains of Indian ink

The calibre of the periosteal blood vessels and their number were highly dependent upon the bone formation activity of the periosteum On formation of *primary osteones, relatively wide, somewhat tortuous blood vessels* were seen to cross each other in several layers On formation of circumferential lamellar bone the blood vessels were narrow and straight throughout and the vascular layer thinner On completion of bone formation only occasional narrow vessels were seen in the subperiosteal layer

In the growing animals the blood vessels in the subperiosteal bone were usually relatively wide in calibre and in some cases two vessels were found in the same bone canal The bone canals in the middle part of the cortex *usually contained only one blood vessel At this location two vessels in the* same canal were only observed following so called cutter heads in the formation of secondary osteones (Color pl 3 *a*) In the growing animals the bone canals around the blood vessels were often considerably wider than the enclosed vessel,but in the adults the bone canal was only very slightly wider than the blood vessel In the subendosteal bone two blood vessels were sometimes found in the same bone canal In these cases one of the vessels was often wide and its walls lined with grains of Indian ink while the other was narrow *and massively filled* with the dye *The former vessel* was considered to be a venule and the latter an arteriole

Microangiographic Pattern after Reaming of the Medullary Cavity

The material for this study comprised the animals in Table 1 with the exception of 81 on which angiography was not performed

The periosteal vascular pattern varied with the local growth situation of the periosteum Corresponding areas on the treated and control sides always had to be compared therefore before the effect of intra medullary reaming on the periosteal blood vessels could be evaluated

Observation time 0–2 days

Periosteum In all preparations the periosteal blood vessels were massively filled with Indian ink Two of the nine animals (27 28) showed subperiosteal haemorrhages in the area of the insertion of the fibula on the tibia *In the* subperiosteal haemorrhages a small leakage of Indian ink was

Cortex Blood vessels passing from the periosteum into the cortex widened in funnel shape fashion in three of the six young animals (64 66 95) and in one of the three adult animals (121) A tendency to the same reaction was observed in one further young animal (105) The intracortical blood vessels were more massively filled with Indian ink than those observed at 3 days but otherwise had the ame appearance

Medullary cavity Newly formed blood vessels had invaded the medullary cavity in all young animals and in two of the three adults (121 44) In all cases the vessels had only invaded from endosteal surface which had not been damaged by the reamer The vessels which first invaded the medullary cavity comprised a three-dimensional irregularly shaped network of mutu ally anastomosing vessels with pronounced calibre variation In cross sec tion the blood vessels were often polygonal with a diameter of between 2 and 30 μ

Observation time 2 weeks

Periosteum The vascular reactions in the periosteum were similar to those at an observation time of 1 week but as a rule more pronounced (Color pl 2 *a*) Apart from the previously described vascular reactions wide round blood vessels of equal calibre lined with grains of Indian ink were now seen in the deeper parts of the periosteal callus tissue in the areas where the long periosteal vessels perpendicular to the bone surface had for med previously The course of these vessels was essentially parallel to the bone surface This vascular reaction occurred on bone resorption when ca vities were formed in trabecular bone In all of the young animals and in three of the five adults the blood vessels passing from the periosteum into the cortex were dilated

Cortex In the outer part of the cortex many but not all of the intra cortical vessels were dilated In deeper parts of the cortex there were two forms of vascular reaction which could occur within the same section The most common reaction which was observed in all growing and adult ani mals comprised loops of blood vessels forming a ball with a diameter of about 20-35 μ In some cases several vessels could be seen leading to these loops This accumulation of blood vessels appeared to occur at the border between cortical areas in which the vessels had filled with Indian ink on angiography and areas with no Indian ink filling. It comprised the vascular component of a cutter head whi h revascularized the cortex (Color pl 3 *a*) The other vascular rea tion consisted of large broom-shaped bundles of blood vessels inside the cortex or between the original cortex and perio-steal newly formed bone (Color pl 2 *a*) At the base of the vascular broom a narrow massively filled blood vessel and several wider vessels



Fig 22 Distal Spalteholz preparation from ventro-tibial part of cortex observation time 3 days Growing animal 124 Practically all blood vessels in the cortex nearest to the medullary cavity are filled with Indian ink From several vessels in the non reamed part of the cortex extravasation of Indian ink into the medullary cavity blood clot is seen

which opened into the medullary cavity (Figs 11 22) as in preparations at shorter observation times

Observation time 1 week

Periosteum In all animals with the exception of one adult *(126)* periosteal blood vessels were observed which showed changes compared with corresponding areas on the control side The vascular reaction varied In the least pronounced reaction the blood vessels were widened and often more tortuous than on the control side This was observed in the formation of circumferential lamellae In stronger reactions which occurred by formation of primary osteones several layers of dilated and tortuous vessels were seen In the strongest reaction long slightly tortuous vessels were observed with pronounced calibre variation running practically perpendicular to the bone surface The blood vessels anastomosed with each other in a U shaped fashion at varying heights often immediately outside the original cortex These blood vessels were present where trabecular bone was being formed (See color pl 2 *a*)

vessels In two young animals (51 52) cavities were seen in the callus at the insertion of the fibula on the tibia The blood vessels in the cavity showed essentially the same appearance as in normal medullary tissue

Cortex In the outer cortex many of the blood vessels were wider on the treated side than on the control side Several wide vessels often massively filled with Indian ink were seen to run from the periosteum through the cortex to the medullary cavity The Indian ink columns in these vessels were about 40 μ in diameter The cortex lying immediately under the callus cavities was sparsely revascularized by fairly thin blood vessels In the deeper parts of the cortex here there was a complete absence of Indian ink filled vessel

Medullary cavity In all animals blood vessels were seen to emerge from almost all parts of the cortex Wide vessels as a rule veins were observed in three of the seven growing and two of the five adult animals In the centre of the medullary cavity in the growing animals occasional immature blood vessels were seen of the type described at an observation time of 1 week viz polygonal of varying calibre and massively filled with Indian ink Peripheral to this area there was a large number of mutually anastomosing blood vessels of circular cross section and with a diameter of 30–40 μ These vessels formed a network with meshes measuring about 70 μ Woven bone was seen betwe n the vessels In other areas of the medullary cavity there were sparsely located narrow somewhat tortuous vessels of equal calibre which in the form of a brush ran in one direction The tissue structure between these blood vessels appeared on the angiography preparations to be homogeneous Adjacent to the endosteum there were long blood vessels about 100 μ wide with a circular cross section and lined with grains of Indian ink These wide vessels lay in direct contact with intermediately located bone trabeculae (Fig 24) Alternating with these wide vessels adjacent to the endosteum straight vessels about 50 μ thick and massively filled with Indian ink were seen

Blood vessels from the medullary cavity returned to avascular parts of the cortex and revascularized the inner part of the cortex

Observation time 8 weeks

Periosteum The periosteal vascular reaction appeared to have disappeared completely No difference in the width or tortuosity of the blood vessels or of the depth of the vascular layer was found on comparison between the treated and control sides The blood vessels in the newly formed periosteal bone had assumed a completely mature appearance

Cortex The difference between the angiographic pattern in the ou er and inner parts of the cortex was pronounced In the outer cortical regions most

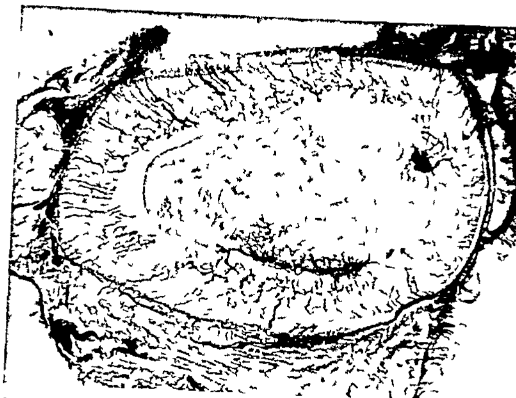


Fig 23 Distal Spalteholz section observation time 2 weeks Growing animal 281 Newly formed blood vessels are seen in the medullary cavity In some areas the endosteal part of the cortex is not yet revascularized

lined with Indian ink were often observed When this vascular reaction occurred from the surface of the original cortex a pronounced vascular reaction was usually observed at the same time in the overlying periosteum

Medullary cavity The vascular reaction in the medullary cavity was similar to that observed at 1 week Newly formed blood vessels were seen in the medullary cavity in all animals except one young animal (45) In only one case (281) (Fig 23) were blood vessels seen to emerge from the cortex at a location where the endosteal bone had been directly damaged by the rotating reamer In the other cases the blood vessels emerged from the cortex in the non reamed areas

Observation time 4 weeks

Periosteum The reaction in the periosteal blood vessels had diminished considerably and was only observed in one of the six young animals (97) and one of the five adults (89) The vascular density in the subperiosteal bone which had developed after the reaming had decreased greatly The blood vessels had also decreased in diameter had become straighter and had assumed essentially the same appearance as the deeper located intracortical

with thick walls were ob erved in all young animals and in three of the six adults In addition to the type of blood vessels described for the 4 week preparations normal sinusoids were also seen in all animals

Observation time 12 weeks

Periosteum The perio teal blood vessels had the ame appearance on the treated side as on the control side

Cortex Three of the five animals showed reva cularized cortex Even in these animals however small areas of central cortex which had not been invaded by blood vessels were seen

Medullary cavity In the medullary cavity in all animals areas with normal sinusoids were found In many animals however there were areas which had not been revascularized The types of blood vessels described for the 4 week and 8 week preparations were also found at this observation time The immature vessels observed at 1 week were not seen in the 12 week preparations however

Discussion

Reaction in Periosteum

Three days after reaming of the medullary cavity a distinct reaction was observed in the periosteal blood vessels especially in the young animals These blood ve sels had become wider and more tortuous and were filled more massively with Indian ink than on the control side Koekenberg (1963) observed this va cular reaction one week after fra ture in the rabbit tibia He called these vessels type 1 and considered that they represented hyperaemia in existing blood vessels

The blood vessel type which Koekenberg named type 2 consisted of mutually parallel vessels perpendicular to the bone surface which initially showed varying calibres but whi h after about 2 weeks were found to be of equal width Koekenberg found this vascular reaction in his preparations 2 and 4 weeks after fracture in the rabbit tibia In the present material such blood vessels were observed between periosteum and cortex in those cases where fluorescen e preparations showed that trabecular bone had been formed The underlying cortex was then as a rule avascular Göthman (1961) observed this vascular reaction subperiosteally 2–6 weeks after nailing of rabbit tibias without fracture "in only a few cases" The typical pattern with blood vessels of type 2 is eliminated when the bone is reconstructed A similar vascular reaction can sometimes be een in the medullary cavity on the formation of a homogeneous fibrous tissue In the present



Fig 24 Proximal Spalteholz cross section observation time 4 weeks Growing animal 15 Three different vascular areas can be seen in the medullary cavity Nearest to the central extravasation of Indian ink there are small areas penetrated by narrow vessels (*fibrotic areas*) Peripheral to these areas there is a broad zone of wider vessels between lighter zones (bone trabeculae) Nearest to the endosteum a small number of light zones (bone trabeculae) surrounded by wide Indian ink filled vessels are seen In the innermost part of the cortex resorption cavities are observed especially fibularly

vessels showed a normal appearance but some wide vessels connecting the *vessels of the periosteum and those of the medullary cavity were observed* In the inner part of the cortex a large number of wide vessels were found often located in resorption cavities in the bone These blood vessels communicated with the medullary cavity by a large number of vessels of fairly wide calibre Blood vessels were found in almost the entire cortex in all growing and in two of the six adult animals but between the vessels in the inner part of the cortex there were small areas of bone tissue which were not revascularized In this area several bone canals contained two blood vessels one of which was narrow and massively filled with Indian ink while the other was wider with Indian ink only lining its walls

Medullary cavity Blood vessels were found in the medullary cavity in all animals In all animals except one (83) blood vessels were seen to have invaded the medullary cavity even from *endosteal bone which had been* damaged by the reamer Vessels of wide calibre in some cases arteries

with thick walls were observed in all young animals and in three of the six adults In addition to the type of blood vessels described for the 4 week preparations normal sinusoids were also seen in all animals

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study the vascular reaction in the periosteum was most pronounced at an observation time of 2 weeks it had decreased at 4 weeks and was completely absent at 8 weeks

At observation times of less than 1 week subperiosteal haemorrhages were often seen within the area of insertion of the fibula on the tibia As a rule no Indian ink had leaked into these haemorrhages, indicating that they had occurred before the Indian ink angiography Subperiosteal haemorrhages were sometimes also found in other areas of the diaphysis The reason for these haemorrhages will be discussed in chapter 4 On preparations observed at 1 week or later, no subperiosteal haemorrhages were seen and it is probable that they had been resorbed Within the area in which they were usually found trabecular bone was often observed instead

On the resorption of bone trabeculae in the central parts of newly formed trabecular bone under the periosteum, wide, round blood vessels of equal thickness and parallel with the peripheral surface of the original cortex were found These vessels were of the same type as occurred in the medullary cavity on resorption of the bone beams there In both cases this type of blood vessel was often later replaced by normal sinusoids

Reaction in Cortex

The first vascular reaction in the cortex was widening of the blood vessels in that part of the outer cortex in which the blood circulation was still present after reaming of the medullary cavity A tendency towards this reaction was found in young animals at an observation time of 3 days, and the reaction was pronounced at 1 week The blood vessels appeared first to become wider in the bone canals without the latter being changed but later the bone canals also increased in calibre Rhinelander & Baragry (1962) considered that parts of the intracortical capillary network were normally resting but that on increased functional demands e g following a fracture of the contralateral bone the blood vessels opened and thus could be filled with contrast medium Gothman (1961) and Brookes (1964) found that Micropack suspension did not pass into the cortex from periosteal vessels until about 1 week after a disturbance of the endosteal circulation in the rabbit Brookes considered that the intracortical vessels increased in calibre due to reversal of the normal blood flow The present experiments indicated that immediately after reaming of the medullary cavity the blood vessels passing from the periosteum into the cortex were able to lead blood into the cortex and that these vessels then became successively wider The deficiency in vascular filling with contrast medium observed by Rhinelander & Baragry and other workers was probably due to the fact that Micropack

has difficulty in passing through these blood vessels before they have increased in calibre which does not take place to a sufficient degree until about one week after the operation Some of the blood vessels in the outer cortex continued to increase in width during the 12 weeks of the present experiments Other vessels which had increased in size during the first weeks after the intramedullary reaming appeared to decrease again in calibre after about 4 weeks at the same time as their bone canals became narrower The circulation from the periosteum into the cortex thereby became more and more concentrated to a smaller number of increasingly wide vessels while the majority of blood vessels in the outer part of the cortex got the same appearance as on the control side

The reaction in the inner part of the cortex depended upon whether or not the area had retained its circulation after the reaming In those areas which had retained their circulation the blood vessels appeared to react in the same way as in the outer vascularized part of the cortex From the borderline area between those parts of the cortex in which the blood vessels still functioned after reaming of the medullary cavity and those which no longer functioned special vascular reactions were observed after about 2 weeks These appeared to be of two types either a ball of blood vessel loops was formed which comprised the vacsular component in a cutter head" or a fairly large broom shaped bundle of vessels Around the bundle of blood vessels so much bone was sometimes resorbed in young animals that a very large cavity was formed in the cortex Arciform blood vessels could then be seen passing to the underlying bone in which resorption was taking place The cutter heads and bundles of blood vessels widened canals or cavities in the direction towards the medullary cavity and in this way revascularized the cortex At this stage their vascular communication was only with the periosteal blood vessels

Reaction in Medullary Cavity

On the first few days after the operation most preparations showed occasional blood vessels which passed from the periosteum through the entire cortex as far as the medullary cavity These vessels were *seen in areas* which had not been damaged directly by the rotating *reamer That these* blood vessels really were functioning for the transport of fluid was shown by fluorescence preparations from animal 124 at an observation time of 3 days *This animal* had been given tetracycline 24 *hours* after the operation The tetracycline had diffused out into the medullary cavity around a blood vessel which had opened on the endosteal *surface* and had become bound to bone fragments immediately outside the vessel The tetracycline

had then not become reabsorbed into the circulation but was visible on the fluorescence preparation The binding of tetracycline to the bone fragments was probably due to the fact that they were becoming halisteretic by lying in an acid environment In the development of halisteresis there is a release of calcium ions, and if these are not removed owing to a poor circulation tetracycline can become bound to them (Eger & Kammerer, 1967) See p 48 Fig 11

The first blood vessels to develop in the medullary cavity were observed at an observation time of 1 week These vessels were irregular in shape and varied in calibre, and formed a three dimensional network They closely resembled the type referred to by Koekenberg as type 3 Koekenberg found type 3 blood vessels during fracture healing in the rabbit at an observation time of 2–7 weeks and considered that they were associated with chondral ossification In the present material they were always the first blood vessels to form on revascularization of subperiosteal haematomas or of the medullary cavity In no preparation was cartilage formation observed Often in places where blood vessels had invaded the medullary cavity from the cortex a narrow blood vessel massively filled with contrast medium which was considered to be an artery was observed, as well as several round blood vessels lined with grains of Indian ink, which were considered to be veins The bone formation in the medullary cavity did not appear to take place in direct association with the types of blood vessel referred to by Koekenberg as type 3, but later when round vessels of medium calibre and anastomosing in network form had developed Within the meshes of the network, between these blood vessels woven bone was formed Resorption of bone trabeculae in the medullary cavity appeared to take place near to 100 μ wide anastomosing round blood vessels which bordered closely on the surface of these beams After resorption of the bone trabeculae the blood vessels underwent a change to apparently normal sinusoids

On Indian ink filling of intracortical vessels by the method described here, the entire vascular bed including the capillaries became filled The method is therefore suitable when the nutritive flow in the cortex is to be studied, but does not allow determination of the direction of the blood flow on a material not subjected to operation This has also been pointed out by Brookes (1960)

STUDY OF THE EXTENT OF INTRACORTICAL VASCULAR DAMAGE

Previous investigations concerning the capacity of the periosteal vessels to take over the intracortical circulation when the contents of the medullary

cavity have been destroyed have given varying results (see chapter 1) It was therefore considered of interest to study by means of Indian ink angiography and the Spalteholz technique the extent of the intracortical vascular damage that occurs after reaming of the medullary cavity and to follow the revascularization of the cortex Indian ink angiography gives good visualization of the intracortical vessels even one day after the operation and with the Spalteholz technique it is possible to study the Indian ink filling by stereomicroscopy and to record the vascular front (see p 30)

Material and Methods

The material comprised the 67 animals—36 growing and 31 adults— shown in Table 1 which were studied at observation times of 1–3 days 1 week 2 weeks 4 weeks 8 weeks and 12 weeks Animal 81 in which angiography was not performed was not included From animals with observation times of 1–3 day two angiography sections from the diaphysis were examined—one about 2 8 cm and one about 7 3 cm from the tibiotalar joint From the remaining animals ections from the distal part of the diaphysis were examined The percentual part of the original cortex (area *BE*) which lacked Indian ink filled vessels (area *CD*) was recorded

The areas of the section in which the vessels were filled with Indian ink were called vascularized cortex and those which lacked Indian ink filled vessels avascular cortex The borderline between Indian ink filled and non Indian ink filled areas was called the vascular front.

At observation times of 8 and 12 weeks many vessels were observed which first penetrated through the cortex into the medullary cavity and then invaded the cortex within another area The cortex was thus revascularized also from the medullary cavity Vessels were then found in the cortex both close to the medullary cavity and in the outer part but interlying areas of the cortex could lack blood ves el In these cases the assessment of the surface of avascular bone on the basis of the vascular front was not reliable and the percentual part of the cortical surface which was avascular had to be estimated instead

Results

The mean values of the percentage of avascular cortex within each experimental group are given in Table 3 *a* for growing animals and in Table 3 *b* for adult animals The tables also show the ranges of variation within the different groups

From the table for growing animals can be seen that in the group observed at 1–3 days 26 % of the cross section area of the cortex was avascu

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The vascular damage in the cortex was possibly somewhat greater in the adults than in the growing animals Since the vessels in the subperiosteal bone are narrower in the adults than in the growing animals this difference may be due partly to the fact that the Indian ink suspension did not fill the intracortical vessels so completely in the adult animals despite the fact that these had functioned intravitally

The variations in that part of the cortex which became avascular between the different animals and between different sectors in the same animal was so great that the avascularity could not have been due solely to occlusion of the blood supply from the medullary cavity but must also have had other causes This will be discussed in chapter 4

At an observation time of 8 weeks the cortex in the growing animals was completely revascularized This finding was made by Trueta & Cavadias

Table 3 a b *Mean value and variation range of the percentage of avascular cortex (CD 100/BE) in individual sectors and whole sections in experimental groups studied at observation times of 1 day to 8–12 weeks*

P indicates the proximal section and *D* the distal section

Obs time	No of animals	Section	1 (Tibial) ( )	2 (Dorsal) ( )	3 (Fibular) ( )	4 (Ventral) ( )	5 (Total) ( )
a *Growing animals*							
1–3 d	8	P	20 (7–38)	24 (2–40)	32 (7–56)	35 (16–50)	26 (12–37)
1–3 d	8	D	32 (0–80)	22 (12–43)	24 (4–64)	28 (13–57)	26 (9–61)
1 w	6	D	19 (3–41)	15 (5–29)	13 (3–28)	16 (5–25)	16 (8–25)
2 w	10	D	32 (5–84)	29 (8–60)	26 (5–71)	25 (8–60)	28 (8–67)
4 w	7	D	14 (0–37)	10 (0–38)	7 (0–27)	10 (0–25)	11 (0–26)
8 w	5	D	0	0	0	0	0
b *Adult animals*							
1–3 d	7	P	39 (5–66)	29 (15–52)	41 (3–66)	51 (4–78)	40 (8–58)
1–3 d	7	D	34 (8–67)	28 (0–67)	33 (7–58)	25 (12–43)	31 (10–50)
1 w	3	D	34 (11–67)	28 (15–40)	23 (2–58)	23 (13–38)	26 (11–5?)
2 w	5	D	26 (2–80)	18 (5–46)	14 (0–32)	17 (9–30)	19 (4–44)
4 w	5	D	27 (1–48)	22 (12–38)	14 (5–26)	30 (2–72)	24 (5–41)
8 w	6	D	6 (0–30)	1 (0–5)	0	7 (0–15)	4 (0–?0)
12 w	5	D	0	6 (0–30)	4 (0–20)	10 (0–40)	7 (0–15)

lar The avascularity was fairly evenly distributed within the four sectors The values for the proximal and the distal sections corresponded well The range of variation was very wide in the distal section between 9 % and 61 % The variation was smaller in the proximal sections In one animal (125) the whole of the tibial sector of the distal section was vascularized At observation times of longer than 2 weeks there was a tendency for a smaller part of the cortex to be avascular Thus at 4 weeks there were two animals in which the whole of the cortical cross section area was revascularized (7 216) and at 8 weeks all growing animals showed complete revascularization of the cortex

The adult animals had a somewhat higher mean percentage of avascular cortex at an observation time of 1–3 days both in the distal and proximal section than the growing animals Also in the adult group a very large variation was found between individual animals There was some tendency for the lowest percentage of avascular cortex in any animal in an experimental group to decrease with increasing observation times At an observation time of 8 weeks two animals showed completely revascularized cortex (67 77) while in the others between 5 % and 20 % of the cortex was estimated to be still avascular At 12 weeks two animals (70 76) showed revascularized cortex and in the other three about 10 % of the cortex was avascular

During the first hours after reaming of the medullary cavity incomplete filling of the intracortical vessels is obtained on angiography with Indian ink (see p 67) but after about 24 hours the visualization is so good that the vascular front can be recorded Revascularization of the cortex takes place from residual intracortical vessels which are supplied from periosteal vessels According to Axhausen & Bergmann (1937) the first budding of new vessels on revascularization of a fracture area begins at the end of the second day The percentage of avascular cortex which is recorded on sections at observation times of 1–3 days should therefore give a good reflection of the vascular damage caused by reaming of the medullary cavity In this material about 30 of the cortical cross section was avascular both within the distal and proximal part of the diaphysis If this corresponds to the area of the cortex which cannot be supplied by the periosteal vessels when the medullary cavity is destroyed these findings are in disagreement with several previous results Thus de Marneffe (1953) claims that within the distal part of the tibial diaphysis in the rabbit the cortex is supplied to the largest part from periosteal vessels while in the proximal part of the diaphysis only the outer part of the cortex is supplied from these vessels Trueta & Cavadias (1955) found in rabbits that only the outer third of the cortex was supplied from periosteal vessels and the rest from endosteal vessels In the experimental studies of these latter authors however considerable pressure may have occurred in the medullary cavity when the metaphyses were plugged which may have caused damage to the intracortical vessels (see p 110) As a perfusion medium they used mainly Micropack which probably gives poorer filling of the cortical vessel than Indian ink These factors may explain their different results

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(1955) after an observation time of 7 weeks in growing rabbits In adult rabbits avascular parts of the cortex were still seen in many cases after observation times of both 8 and 12 weeks

STUDY OF THE AMOUNT OF NEWLY FORMED PERIOSTEAL BONE

Material

The material consisted of 39 rabbits 22 of which were growing animals and 17 adults The material comprised those animals in Table 1 in which *one* tibia was operated on the other tibia serving as a control The observation times, i e the lengths of time after the operation to the angiography, were 1 2, 4 and 8 weeks Growing animals in which labelling I (see p 25) was performed at time points 0–2 days after reaming of the medullary cavity and adult animals in which labelling 1 was performed 1–4 days after the operation were included The two growing animals, 6 and 7 and the adult animal 75, in which labelling 1 was not performed until 7 days after the reaming were thus not included

Method

The area of the newly formed periosteal bone (area *AB*) was calculated on the distal transverse fluorescence section from approximately 3 3 cm above the tibiotalar joint (see p 36) Area *AB* is expressed as a percentage of the area of the original cortex (area *BE*) The calculation was made separately for each sector and also for the whole cross section on the treated side and on the control side In the calculation of the whole cross section the sum of *AB* from the four sectors is expressed in per cent of the sum of *BE* from the four sectors A sector from the treated side and the corresponding sector from the control side are called a pair of sectors The section from the treated side and the section from the control side are called a pair of sections The percentage value obtained for the periosteally formed new bone is called within each sector the bone formation value (BF) The mean bone formation value for all animals in an experimental group is denoted the mean bone formation (MBF) The term Z is added when the whole cross section has been calculated the term C when the calculation refers to the control side and O when it refers to the reamed side For example MBFZC = mean bone formation for the whole sections on the control side in one experimental group

The difference between the bone formation values on the treated and control sides within each pair of sectors is called the bone formation difference (BFD) The mean bone formation difference for all animals in an experimental group is denoted the mean bone formation difference (MBFD) The term Z is used in the same way as in the calculation of the bone formation values

Significance testing of the difference in periosteal bone formation between the main experimental groups was performed by means of the Wilcoxon test (see *Documenta Geigy* 6th ed p 124)

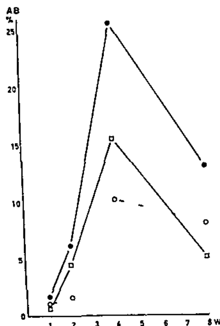


Fig 25 Growing animals Mean periosteal bone formation (area *AB*) in per cent of the area of the original cortex (area *BE*) in the whole section in the experimental groups with observation times of 1 to 8 weeks ●—● treated bone (MBFZO) ○ ○ control bone (MBFZC) □—□ difference between treated and control bone (MBFDZ)

Results

Growing Animals (Fig 25)

Observation time 1 week MBFZC was 1 1° BFZC varied between the individual animals from 0 4–1 6

MBFDZ was 0 6 ⁄ BFDZ varied between the individual animals from 0 1 to 1 3 ₀ MBFD was greatest in the ventral sector (0 9°) and smallest in the fibular sector (0 3) BFD was greatest (1 8 ⁄) in the tibial sector in animal 95 and smallest (−0 2°') in the dorsal and tibial sectors in animal 106

Observation time 2 weeks MBFZC was 1 6 BFZC varied between the individual animals from 0 4 to 3 0 %

MBFDZ was 4 5 ⁄ BFDZ varied between the individual animals from 0 3 to 10 5 % MBFD was greatest in the fibular sector (8 2°') and smallest in the ventral sector (2 8) BFD was greatest (31 1) in the fibular sector in animal 281 and smallest (−0 1) in the ventral sector in animal 101

Observation time 4 weeks MBFZC was 10 2% BFZC varied between the individual animals from 3 2% to 33 5%

MBFDZ was 15 5% BFDZ varied between the individual animals from 0 4 to 60 8% MBFD was greatest in the fibular sector (20 5%) and smallest in the tibial sector (8 5%) BFD was greatest (82 0%) in the fibular sector in animal 52 and smallest (−1 4%) in the ventral sector in animal 216

Observation time 8 weeks MBFZC was 8 1% BFZC varied between the individual animals from 2 6 to 19 7%

MBFDZ was 5 0% BFDZ varied between the individual animals from 3 0 to 8 0% MBFD was greatest in the fibular sector (8 2%) and smallest in the tibial sector (2 7%) BFD was greatest (15 8%) in the dorsal sector in animal 111 and smallest (−0 2%) in the tibial sector in animal 65

In the group observed at 1 week only small amounts of bone had been formed subperiosteally, both on the treated and the control side

On comparison between the groups observed at 1 and 2 weeks, an increase in the area of newly formed bone was found on the treated side, which was significant at the 5% level while the bone area on the control side had increased only very slightly A significant difference at the 10% level was found between the treated and the control side in the group observed at 2 weeks

On comparison between the groups observed at 2 and 4 weeks, a further increase in the mean bone area on the treated side was found This increase was due largely to the considerable bone formation in one animal (52) and is not significant On the control side the bone area had increased significantly at the 1% level on comparison between the same groups of animals No significant difference was found between the treated and control side in the group observed at 4 weeks

Comparison between the groups of animals observed at 4 and 8 weeks showed no significant difference in the area of newly formed bone either on the treated or on the control side

Adult Animals (Fig 26)

Observation time 1 week MBFZC = 0 2% BFZC varied between the individual animals from 0 to 0 7%

MBFDZ was 0 4% BFDZ varied between the individual animals from 0 1 to 0 9% MBFD was greatest in the ventral sector (0 7%) and smallest in the fibular sector (0 0%) BFD was greatest (2 1%) in the ventral sector in animal 121 and smallest (−0 1%) in the fibular sector in animal 121

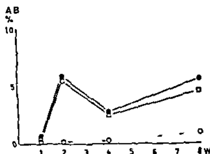


Fig 26 Adult animals Mean periosteal bone formation (area *AB*) in per cent of the area of original cortex (area *BE*) in the whole section in the experimental groups with observation times of 1 to 8 weeks (For notation see Table 25)

Observation time 2 weeks MBFZC was 0 2° BFZC varied between the individual animals from 0 0 to 0 8 %

MBFDZ was 5 5°, BFDZ varied between the individual animals from 0 3 to 21 8 ′ MBFD was greatest in the dorsal sector (7 1 ′) and smallest in the ventral sector (2 9%) BFD was greatest (24 3%) in the dorsal sector in animal 86 and smallest (−0 2 ′) in the fibular sector in animal 58

Observation time 4 weeks MBFZC was 0 3 ° BFZC varied between the individual animals from 0 to 1 0°

MBFDZ was 2 5 % BFDZ varied between the individual animals from 0 3 to 6 9° MBFD was greatest in the tibial sector (4 7) and smallest in the fibular sector (1 3°) BFD was greatest (16 7%) in the tibial sector in animal 89 and smallest (0 0) in the dorsal sector in animal 88

Observation time 8 weeks MBFZC was 1 0 BFZC varied between the individual animals from 0 7 to 1 6

MBFDZ was 4 6 ° BFDZ varied between the individual animals from 1 2 to 7 6 % MBFD was greatest in the ventral sector (7 2 /) and smallest in the fibular sector (2 9 %) BFD was greatest (13 3°) in the dorsal sector in animal 85 and smallest (0 1) in the dorsal sector in animal 77

On comparison between the groups observed at 1 and 2 weeks and between those observed at 2 and 4 weeks no significant difference in the area of newly formed bone was found either on the treated or the control side The high mean value for the bone formation on the treated side at an observation time of 2 weeks was mainly due to the large amount of new bone formed in one animal 86

Comparison of the bone formation in the combined groups observed at 1 2 and 4 weeks with that in the group observed at 8 weeks showed a significant increase at the 5 % level on the treated side and a significant in

crease at the 2 % level on the control side The difference in area of newly formed bone between the treated side and control side on comparison between these groups was significant at the 10 % level

Discussion

With the method of recording used, measurements were made of the cross sectional area of the periosteal tissue whose bone component was mineralized within 8 hours after labelling 2 (see p 33) This area comprised bone tissue with varying percentages of vessels and perivascular tissue (vascular tissue) If circumferential lamellae has been formed there is approximately the same percentage of vascular tissue as in normal cortical bone If primary osteones have been formed there is a high percentage of vascular tissue when the osteones are newly formed The percentage of vascular tissue decreases continuously when the osteones mature and after about 4 weeks the bone tissue has the same percentage of vascular tissue as normal cortical bone If trabecular bone has been formed the development of the bone tissue can vary In one case the trabecular bone can be condensed to compact bone and then has a normal percentage of vascular tissue In another case the central parts of the trabecular bone can instead be broken down and replaced by a richly vascularized cavity (see p 62)

That part of the area of the newly formed bone which consists of actual bone tissue will therefore be dependent upon the length of the observation time and the morphology of the bone

In this series of experiments the variations between the individual animals in the experimental groups and between the different sectors in the same animal were considerable In all growing and adult animals the periosteal bone formation in the whole section was greater on the treated than on the control side In individual pairs of sectors the bone formation was greater on the treated side than on the control side in 82 of the 88 pairs of sectors in growing animals and in 65 of the 68 pairs of sectors in adult animals Evaluation of the significance of the difference between the different experimental groups was therefore not made on the basis of the mean values and distribution of the mean values of the groups but according to the Wilcoxon test using the order of rank of the measurement values obtained

After causing a disturbance of the endosteal circulation of the long bone many authors have observed increased periosteal bone formation (Axhausen & Bergmann 1937 Rohlich 1941 Trueta & Cavadias 1955 Kuntscher 1957, Richany *et al* 1965 Mital & Cohen 1966 Flatmark 1967 Zucman *et al* 1968) These investigators have assessed the increased bone

mass histologically or by repeated radiographic studies during the course of the experiment

With histological techniques the boundary between the original cortex and the newly formed periosteal bone can only be established with certainty if the newly formed bone has a different morphology from that of the original cortex As a rule therefore the exact borderline cannot be determined if the newly formed bone comprises circumferential lamellae or primary osteones only with certainty if it is trabecular Acceleration or restimulation of the normal bone formation can then often not be demonstrated with certainty but only the real callus formation

Repeated radiographic examinations during the course of the experiment cannot as a rule reveal minor changes in the bone mass

In this investigation two tetracycline injections were given—one at the start of the experiment and the other at its end In this way the bone formed during the experimental period was delimited By this method even small amounts of bone could be measured Similar techniques for the assessmet of newly formed bone or dentine have been used by Frost (1963) Tapp (1966) Hansson (1967) and Ahlgren (1968) There appear to have been no previous reports in the literature on the use of bone labelling techniques in studies of the amount of periosteal bone formation after disturbances of the endosteal circulation of the long bone

During the first week after reaming of the medullary cavity in growing animals only very small amounts of new bone were formed subperiosteally both on the treated and the control side This first week comprises the adrenergic corticoid postoperative phase for the animal during which an increased quantity of adrenocortical steroids are released which on experimental administration have been found to result in depression of the bone formation (Hulth & Olerud 1964 Tapp 1966) The main bone formation on the treated side in growing animals takes place during the second week of the experiment which should comprise the anabolic postoperative phase On the control side the main bone formation takes place during the third and fourth weeks postoperatively when the bone formation on the treated side is already declining At this time the compensation for the previously retarded formation of bone on the control side can begin

In adult animals the development is more difficult to evaluate No definite increase in the bone formation is evident between subsequent animal groups either on the treated or the control side

The results obtained here for growing animals are in agreement with the findings of Richany *et al* in 1965 By histological methods they observed in young adult cats that after cleaning of the medullary cavity in the femur the bone mass newly formed periosteally was maximal after an observation

time of 3 weeks and was reduced after a further 3 weeks In the present material there was no markedly greater bone formation in any particular sector, as was found by Richany *et al* in the region around the linea aspera.

The difference in bone formation within the different pairs of sectors in an individual animal was sometimes greatest within that pair of sectors where, on the treated side, the vascular damage in the underlying cortex was greatest, or where the largest amount of bone had been removed from the endosteal surface The possible relationship between the amount of newly formed bone and the degree of damage to the underlying cortex will be discussed further in chapter 5

STUDY OF THE BONE FORMATION ACTIVITY OF THE PERIOSTEUM

After reaming of the medullary cavity the periosteum of the bone is as a rule, activated to increased bone formation The bone formation activity was assessed in the present study by (*a*) recording in each sector whether the outer fluorescent band which occurred from labelling 2 was present or not and (*b*) measuring in each sector the thickness of this fluorescent band together with bone and osteoid located peripherally to it

The outer fluorescent band comprises essentially that bone which has been mineralized within 8 hours after the last tetracycline injection (Tapp 1966) The bone and osteoid tissue lying peripheral to the outer fluorescent band was formed during the last 40 hours before the angiographic examination since this examination was performed 2 days after labelling 2 The observed thickness was thus an expression of the bone formation wich had taken place during the days immediately preceding the angiographic examination in contrast to the total bone formation which referred to the whole observation time The measurements were performed with a Zeiss ocular micrometer on the distal transversal fluorescence section at a magnification of 320 times

The periosteum can be activated at different time points after the operation in different animals and in different sectors in the same animal, and the activity can be of varying strengths Each sector must therefore be evaluated separately A sector on the treated side and the corresponding sector on the control side have been called a pair of sectors To obtain a better idea of the bone formation activity of the periosteum this was studied with the aid of several variables, which are defined below Thus for each sector and pair of sectors respectively recordings were made of the activity value (A) activity difference (AD) resorption value (R) resorption difference (RD) absolute growth value (G) absolute growth difference (GD) and stan

dardized growth difference (SGD) The mean value for these variables was calculated for all sectors or pairs of sectors in each individual animal and for all sectors or pairs of sectors in all animals in each experimental group

In this series of experiments the aim was to determine in relation to the time of operation (1) when the periosteal bone formation started to increase (2) when the periosteal bone formation was maximal (3) when the difference in bone formation activity between the treated and the control side was maximal and (4) how long the increased bone formation activity persisted

Material

The material consisted of 49 rabbits 28 of which were growing animals and 21 adults These animals comprised those shown in Table 1 in which one tibia was subjected to operation while the other served as a control and for which the observation times were 3 days and 1 2 4 and 8 weeks The five animals 50 56 85 77 and 92 in which no fluorescent bone was observed after labelling 2 were excluded from the material (see p 34)

Methods

Determination of Activity Values and Activity Differences

When the outer fluorescent band occurred in any part of the middle [illegible] of a sector this sector was called active and when it did not this sector was called inactive An active sector was given the value 1 and an inactive sector the value 0 The value thus given to a sector was called the activity value (A) of the sector A could thus have the value 0 or 1 The mean activity on the treated side or the control side for all four sectors in the same animal was denoted MA MA could have any of the values 0 [illegible] or 1 The mean activity for all sectors in all animals in an experimental group was denoted MAT (= *mean activity total*) MAT could have values between 0 and 1

The difference within a pair of sectors between the activity value on the treated side and that on the control side was denoted the *activity difference* (AD) AD was given the value +1 if the treated side was active and the control side inactive the value −1 if the treated side was inactive and the control side active and the value 0 if both sides were inactive or both active The activity difference for a pair of sectors (AD) could have any of the values −1 0 or +1 The mean activity difference for all four pairs of sectors in one animal was denoted MAD MAD could have any of the values −1 [illegible] 0 [illegible] or +1 The mean activity difference for all pairs of sectors in all animals within an experimental group was denoted MADT MADT could have values between −1 and +1

A regression analysis was performed of the relation of the activity values and activity differences to the observation times these values or differences being used as dependent or *y* variables and the length of the observation time and the square of the length of the observation time as independent or *x* variables In the regression ana

lysis an observation time of 3 days was given the value 1 1 week the value 2 2 weeks the value 3 4 weeks the value 4 and 8 weeks the value 5 The calculations were performed by means of a computer (Uppsala Computer Centre)

Determination of Absolute Growth Values and Absolute Growth Differences

In each sector the maximal thickness of the outer fluorescent band together with bone and osteoid lying peripheral to it was measured within the middle $4/5$ of the sector For each sector the value obtained on measurement was called the absolute growth value (G) The mean of the absolute growth values for all four sectors in the same animal was called the mean absolute growth value (MG) The mean of the absolute growth values for all sectors in all animals in one experimental group was denoted MGT The difference between the absolute growth values on the treated and control sides in each pair of sectors was called the absolute growth difference (GD) The mean of the absolute growth differences for all four sectors in the same animal was called the mean absolute growth difference (MGD) The mean of the absolute growth differences for all four sectors in all animals in an experimental group was denoted MGDT

Determination of Standardized Growth Difference

In a simple calculation of the mean value for the differences in growth values between the treated and control sides high values within individual sectors e g animal 125—dorsal sector will dominate For this reason quantitation of the growth difference to +1 −1 and 0 was performed This was called for each pair of sectors the standardized growth difference (SGD) This was given the value +1 when the thickness on the treated side was significantly greater than on the control side −1 when the thickness on the control side was significantly greater than on the treated side and 0 when the thicknesses on the two sides were the same (see below) SGD could thus be given any of the values 1 0 or −1 The mean value of the standardized growth difference for all pairs of sectors in one animal was denoted MSGD MSGD could have any of the values ± 0 $\pm 1/4$ $\pm 1/2$ $\pm 3/4$ or ± 1 The mean standardized growth difference for all four pairs of sectors in all animals in one experimental group was denoted MSGDT and could have values between −1 and +1

Determination of Resorption Values and Resorption Differences

When resorption was found within more than half of the periphery of a sector this sector was called a sector undergoing resorption and was given the value 1 while a sector not undergoing resorption was given the value 0 The value given was called the resorption value of the sector (R) The mean resorption values (MR and MRT) the resorption difference (RD) and the mean resorption differences (MRD and MRDT) were defined and calculated analogously to the corresponding variables used in assessment of the activity

The resorption could only be evaluated in the growing animals since signs of superficial resorption were very unreliable in the adults

Discussion of the Method

In order to assess when the measured growth difference between the right and left side was greater than the expected spontaneous growth difference

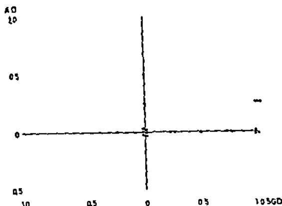


Fig 27 Growing animals Correlation between values of activity difference (AD) and standardized growth difference (SGD) in individual animals Coefficient of correlation (R) = 0 21

between the sides the growth difference was studied in five growing rabbits which did not undergo operation The animals were given tetracycline 2 days before the angiographic examination The thickness of the newly formed bone was measured in the same way as in the experimental series The maximal difference of the thicknesses between the sectors within the pairs of sectors was 1 unit (U) = 3 5 μ see p 32 Only if one of the sectors in a pair was inactive during simultaneous resorption and the other was active did the maximal difference amount to 2 units In this series of experiments it was therefore required that in comparisons between sectors in a pair of sectors the difference in the measured thicknesses should be at least 1 unit for an estimated standardized growth difference to be said to exist If one of the sectors was inactive during simultaneous resorption while the other was inactive the difference should be at least 2 units

In animals observed at 1 week the fluorescent bands from labellings 1 and 2 were usually confluent Also the width of the inner fluorescent band from labelling 1 was therefore taken for measurement of the thickness Since all young animals had a positive activity value in all sectors at an observation time of 3 days it was required in these cases that the thickness should be more than 1 unit for the sector to be considered to have a positive activity value at an observation time of 1 week The criterion for a positive standardized growth difference was that the difference in thicknesses should be at least 2 units On evaluation of the absolute growth the whole value obtained for the thickness was used in the calculation The group of animals observed at 1 week was attributed little importance in the study

An analysis was performed of the correlations (a) between the activity

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Determination of Standardized Growth Difference

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The resorption could only be evaluated in the growing animals since signs of superficial resorption were very unreliable in the adults

Discussion of the Method

In order to assess when the measured growth difference between the right and left side was greater than the expected spontaneous growth difference

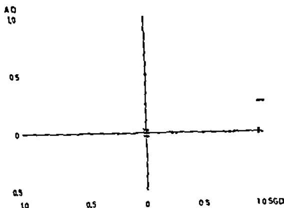


Fig 27 Growing animals Correlation between values of activity difference (AD) and standardized growth difference (SGD) in individual animals Coefficient of correlation $(R) = 0\ 21$

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Determination of Resorption Values and Resorption Differences

When resorption was found within more than half of the periphery of a sector this sector was called a sector undergoing resorption and was given the value 1 while a sector not undergoing resorption was given the value 0 *The value given was called* the resorption value of the sector (R) The mean resorption values (*MR and MRT*) *the* resorption difference (RD) and the mean resorption differences (MRD and MRDT) were defined and calculated analogously to the corresponding variables used in assess *ment of the activity*

The resorption could only be evaluated in the growing animals since signs of super ficial resorption were very unreliable in the adults

Discussion of the Method

In order to assess when the measured growth difference between the right and left side was *greater than* the expected spontaneous growth difference

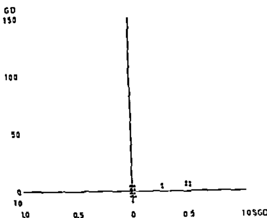


Fig 29

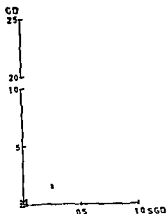


Fig 30

Fig 29 Growing animals Correlation between values of growth difference (GD) and standardized growth difference (SGD) in individual animals Coefficient of correlation (R) = 0 64

Fig 30 Adult animals Correlation between values of growth difference (GD) and standardized growth difference (SGD) in individual animals Coefficient of correlation (R) = 0 69

Studies of the Activity Values

Growing animals

For the control side the regression curve for the activity values (A) of the individual sectors was a downward convex parabola which was found to have different strengths in different sectors For the dorsal and tibial sectors the parabolic form is almost significant but for the ventral and fibular sectors there was only a suggestion of this parabolic form On the treated side there was a tendency to the same parabolic form in the ventral and dorsal sectors but not in the tibial and fibular sectors In the regression curve for AD (see Table 6) the tendency to a more curved form on the control side was strongly evident For the ventral and tibial pairs of sectors there was an upward convex almost significant parabola and in the dorsal and fibular pairs of sectors a suggestion of a parabola of the same appearance At time point 2 8 (an observation time of 12 6 days) and around this point the AD values were almost significantly increased throughout, which is evident from the coefficient of intercept At time point 2 8 AD was 0 34 for the ventral sector 0 19 for the dorsal sector 0 31 for the tibial sector and 0 29 for the fibular sector

The time point for the parabolic maximum was calculated from the formula $t_m = 2\,8 - B/2$ which was obtained by derivation of the equation

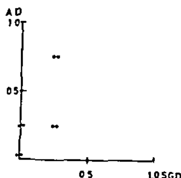


Fig 28 Adult animals Correlation between values of activity difference (AD) and standardized growth difference (SGD) in individual animals Coefficient of correlation $(R) = 0\ 41$

difference (AD) and the standardized growth difference (SGD) and (*b*) be tween the absolute growth difference (GD) and the standardized growth difference (SGD)

In growing animals the correlation coefficient (*r*) between AD and SGD was 0 21 (Fig 27) There was thus a correlation between these methods of recording but it did not reach the significance level The weakness of the correlation is due to the fact that activity was also present on the con trol side in many cases with a positive standardized growth difference especially in animals with a short observation time AD would then be equal to 0, but SGD would be greater than 0

In adult animals the correlation coefficient (*r*) between AD and SGD was 0 41 (Fig 28) The correlation was thus stronger than in the growing ani mals but did not reach the significance level The relatively low *r* value is due to the fact that an activity difference was found in many sectors espe- cially in animals with long observation times, where the thickness measured was so small that only small standardized growth differences occurred

The ratio of the mean value of AD SGD was 0 33 for growing animals and 1 25 for adult animals which also illustrates that the reason for the low *r* value differed partly in growing and adult animals

The correlation between GD and SGD reached a significant level in both growing and adult animals (*Figs 29 30*) *This is a consequence of the* definition of SGD The diagram shows however that when SGD = 1 there was considerable variability of GD expecially in the growing animals

Results

The values obtained on measurement are given in Tables 4 and 5

		Sectors							
		Tibial		Dorsal		Fibular		Ventral	
Obs time	Animal no	*t*	*c*	*t*	*c*	*t*	*c*	*t*	*c*
4 weeks	75	0	0	0	0	0	0	0	0
	88	0	0	0	0	0	0	0	0
	89	4	0	4	0	4	0	4	0
	100	0	0	0	0	0	0	1	0
	113	0	0	1	0	0	0	1	0
8 weeks	67	1	1	0	0	0	0	0	0
	83	0	0	0	0	0	0	1	0
	84	4	0	1	0	0	0	1	0

for the parabola $y = A + B\ (t-2\ 8) + C\ (t-2\ 8)$ In the regression curve for AD the time point for the parabolic maximum for the ventral sector was 2 6 for the dorsal sector 2 7 for the tibial sector 2 6 and for the fibular sector 3 3 The difference between the time points for the parabolic maximum within the different sectors was not significant No evident difference was found in the form of the regression curve for AD between the sum of the reamed sectors (ventral + dorsal) and the sum of the non reamed sectors (tibial + fibular)

Since no marked difference was found between the different sectors or pairs of sectors it seemed suitable to study all sectors combined The regression curve for MAD (Table 6 Fig 31) was an ascendingly convex almost significant parabola with its maximum at time point 2 75 At time

Table 6 *Results of regression analysis for growing animals with activity difference (AD MAD) as dependent variable and length of observation time as independent variable*

The regression equation is written $(AD\ MAD) = A + B\,(t-2\ 8) + C(t-2\ 8)^2$ A coefficient of intercept at $t = 2\ 8$ B regression coefficient for the linear term $(t-2\ 8)$ C regression coefficient for the term $(t-2\ 8)$ The results are given for the difference in each pair of sectors and for the sum of the differences within all 4 pairs of sectors divided by 4 (Mean MAD) denotes the degree of significance

	Sectors									
	Tibial		Dorsal		Fibular		Ventral		Mean	
	Coeff	± S.E.	Coeff	± S.E.	Coeff	± S.E.	Coeff	± S.E.	Coeff	+ S.E.
A	0 31	0 10	0 19	0 08	0 ‑9*	0 10	0 34	0 11	0 29*	0 06
B	0 06	0 06	−0 01	0 05	0 08	0 06	−0 05	0 06	0 01	0 03
C	0 14*	0 05	−0 06	0 04	−0 07	0 05	−0 13	0 05	0 10	0 03

Tables 4 5 *The measured thickness in each sector on the distal fluorescent section of the fluorescent band from the tetracycline labelling given 2 days before sacrifice, together with bone and osteoid located peripherally to it*

Observation time 3 days to 8 weeks after reaming of the medullary cavity *R* indicates that the sector is undergoing resorption *t* = treated side *c* = control side

		Sectors							
		Tibial		Dorsal		Fibular		Ventral	
Obs time	Animal no	*t*	*c*	*t*	*c*	*t*	*c*	*t*	*c*
Growing animals									
3 days	3	3	1	20	3	5	4	24	3
	81	10	6	25	7	8	6	35	10
	114	5	5	5	3	5	4	4	4
	123	1	2	3	3	3	3	2	2
	124	3	3	4	3	4	3	4	3
	125	30	3	70	3	15	3	26	3
1 week	64	8	5	8	5	6	4	15	4
	66	6	5	10	5	6	6	7	6
	95	6 *R*	1 *R*	6	3	9	3	27	7
	104	2	2	3	2	3	4	4	3
	105	7	3	15	4	6	3	25	1
	106	1	1	2	1	2	2	3	1
2 weeks	6	3	0 *R*	0 *R*	0 *R*	3	0 *R*	2 *R*	2
	59	3	0 *R*	0 *R*	0 *R*	3	0 *R*	3 *R*	3 *R*
	101	4	3	5	1	5	1	0	0
	108	0 *R*	0 *R*	0 *R*	0 *R*	0 *R*	0 *R*	1 *R*	0 *R*
	211	7	1	6 *R*	0 *R*	5	1	9	2
	220	2	1 *R*	4	0 *R*	2	1 *R*	3	1
	281	5	0 *R*	0 *R*	0 *R*	50	0 *R*	6	0 *R*
	285	5	2	5	3	5	2	7	4
4 weeks	7	0 *R*	0 *R*	0 *R*	0 *R*	2	0	1	0 *R*
	51	5	5	3	3	4	0 *R*	4	4
	52	2 *R*	3	4	4	4	4	2 *R*	4
	96	2	2	2	2	3	3	2	2
	97	26	3	29	3	15	3	11	3
	216	0 *R*	0	0	0 *R*	0 *R*	0 *R*	0	0
8 weeks	65	0	2	2	5	3	4	0	2
	111	4	3	4	4	4	4	5	4
Adult animals									
3 days	54	3	1	4	2	3	2	3	2
	55	1	1	2	2	1	1	2	1
	63	0	0	1	0	0	0	2	0
	109	0	0	0	0	0	0	0	0
	110	0	0	0	0	0	0	0	0
1 week	112	0	0	12	0	0	0	1	0
	121	6	1	6	2	2	2	25	4
	126	2	0	0	0	0	0	0	0
2 weeks	57	2	0	3	0	2	0	3	0
	58	4	0	1	0	0	0	1	0
	86	35	0	19	0	20	0	15	1
	87	4	0	25	0	3	0	6	0
	119	3	0	0	0	3	0	2	0

Table 7 *Results of regression analysis for adult animals*

For notation see Table 6

	Sectors									
	Tibial		Dorsal		Fibular		Ventral		Mean	
	Coeff	±S E	*Coeff*	±S E	*Coeff*	±S E	*Coeff*	±S E	*Coeff*	±S E
A	0 66	0 15	0 61*	0 17	0 50	0 13	0 63	0 16	0 60*	0 11
B	0 09	0 07	0 06	0 08	0 06	0 06	0 14	0 08	0 09	0 05
C	−0 15	0 06	−0 10	0 07	−0 14*	0 05	−0 06	0 07	−0 11*	0 04

slope throughout but in all sectors significant activity values were found at time point 2 8

In the regression curves for AD (Table 7) the activity values (A) on the treated side at time point 2 8 and around this point predominate so that an almost significant AD value was then found in all sectors For the tibial and fibular sectors the curve had an almost significant parabolic contour but not for the ventral and dorsal sectors For the tibial sector the parabola had its maximum at time point 3 1 and for the fibular sector at time point 3 0 No evident difference was found in the shape of the regression curve for AD between the sum of the reamed sectors (ventral + dorsal) and the sum of the non reamed sectors (tibial + fibular)

The regression curve for MAD (Table 7 Fig 32) was an upwardly convex almost significant parabola with a maximum at time point 3 2 Already

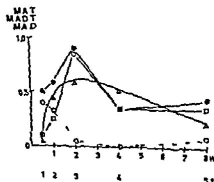


Fig 32 Adult animals. The mean activity value (MAT) and activity difference value (MADT) in each experimental group at observation times of 3 days to 8 weeks and the regression curve for the activity difference (AD) at time points 1 to 5 ●—● MAT for treated tibia ○—○ MAT for control tibia □—□ MADT △—△ regression curve for MAD

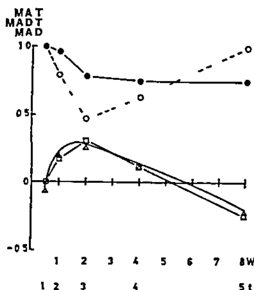


Fig 31 Growing animals The mean activity value (MAT) and activity difference value (MADT) in each experimental group at observation times of 3 days to 8 weeks and the regression curve for the mean activity difference (MAD) at time points 1 to 5 ●—● MAT for treated tibia ○--○ MAT for control tibia □—□ MADT △—△ regression curve for MAD

point 2 8 MAD was 0 29, which is a significantly increased difference value

A study of the relations of the individual experimental groups shows that at an observation time of 3 days MAT = 1 both on the treated and on the control side (Fig 31) On the control side MAT = 0 47 at an observation time of 2 weeks The reduction from 1 to 0 47 was highly significant MAT increased to 0 63 at an observation time of 4 weeks and to 1 0 at 8 weeks This increase is not significant

On the treated side MAT = 0 78 at an observation time of 2 weeks The decrease from 1 0 at an observation time of 3 days to 0 78 at 2 weeks is almost significant At observation times of 4 and 8 weeks MAT = 0 75 The decrease in MAT was so much greater on the control side than on the treated side that MADT was significant at an observation time of 2 weeks

Adult animals

For the control side the regression curve for the activity value (A) of the individual sectors lacked a parabolic shape throughout At time point 2 8 the curve showed a significant downward slope for the dorsal and fibular sectors and a tendency to a downward slope for the ventral sector At this time point none of the sectors on the control side showed a significant A value

For the treated side the regression curve for A lacked a significant para bolic shape throughout. At time point 2 8 the curve showed no significant

Table 7 *Results of regression analysis for adult animals*

For notation see Table 6

	Sectors									
	Tibial		Dorsal		Fibular		Ventral		Mean	
	Coeff	±S.E.	Coeff	±S.E.	Coeff	±S.E.	Coeff	±S.E.	Coeff	±S.E.
A	0.66*	0.15	0.61	0.17	0.50*	0.13	0.63*	0.16	0.60	0.11
B	0.09	0.07	0.06	0.08	0.06	0.06	0.14	0.08	0.09	0.05
C	−0.15	0.06	−0.10	0.07	−0.14*	0.05	−0.06	0.07	0.11*	0.04

slope throughout but in all sectors significant activity values were found at time point 2.8

In the regression curves for AD (Table 7) the activity values (A) on the treated side at time point 2.8 and around this point predominate so that an almost significant AD value was then found in all sectors For the tibial and fibular sectors the curve had an almost significant parabolic contour but not for the ventral and dorsal sectors For the tibial sector the parabola had its maximum at time point 3.1 and for the fibular sector at time point 3.0 No evident difference was found in the shape of the regression curve for AD between the sum of the reamed sectors (ventral + dorsal) and the sum of the non reamed sectors (tibial + fibular)

The regression curve for MAD (Table 7 Fig 32) was an upwardly convex almost significant parabola with a maximum at time point 3.2 Already

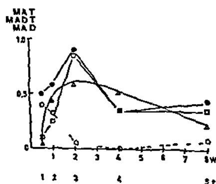


Fig 32 Adult animals The mean activity value (MAT) and activity difference value (MADT) in each experimental group at observation times of 3 days to 8 weeks and the regression curve for the activity difference (AD) at time points 1 to 5 ●—● MAT for treated tibia ○—○ MAT for control tibia □—□ MADT △—△ regression curve for MAD

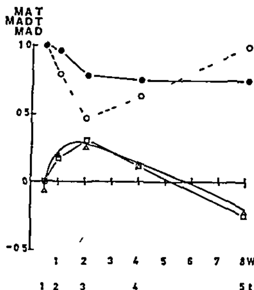


Fig 31 Growing animals The mean activity value (MAT) and activity difference value (MADT) in each experimental group at observation times of 3 days to 8 weeks and the regression curve for the mean activity difference (MAD) at time points 1 to 5 ●—● MAT for treated tibia ○--○ MAT for control tibia □—□ MADT △—△ regression curve for MAD

point 2 8 MAD was 0 29, which is a significantly increased difference value

A study of the relations of the individual experimental groups shows that at an observation time of 3 days MAT = 1 both on the treated and on the control side (Fig 31) On the control side, MAT = 0 47 at an observation time of 2 weeks The reduction from 1 to 0 47 was highly significant MAT increased to 0 63 at an observation time of 4 weeks and to 1 0 at 8 weeks This increase is not significant

On the treated side MAT = 0 78 at an observation time of 2 weeks The decrease from 1 0 at an observation time of 3 days to 0 78 at 2 weeks is almost significant At observation times of 4 and 8 weeks MAT = 0 75 The decrease in MAT was so much greater on the control side than on the treated side that MADT was significant at an observation time of 2 weeks

Adult animals

For the control side the regression curve for the activity value (A) of the individual sectors lacked a parabolic shape throughout At time point 2 8 the curve showed a significant downward slope for the dorsal and fibular sectors and a tendency to a downward slope for the ventral sector At this time point none of the sectors on the control side showed a significant A value

For the treated side the regression curve for A lacked a significant parabolic shape throughout At time point 2 8 the curve showed no significant

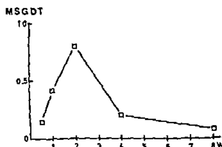


Fig 34 Adult animals Mean standardized growth difference value (MSGDT) in each experimental group at observation times of 3 days to 8 weeks

Study of the Absolute Growth Values

Growing animals (Fig 35)

On the control side MGT was 3 8 U at an ob ervation time of 3 days 0 9 at 2 weeks 2 0 at 4 weeks and 3 5 at 8 weeks On the treated side MGT was 13 1 U at 3 days 4 8 at 2 weeks 5 0 at 4 weeks and 2 8 at 8 weeks On the control side a significantly lower MGT value was found in the animals observed at 2 weeks than in those observed at 3 days and an al most significantly higher MGT value in the animals from the combined groups observed at 4 and 8 weeks compared with those observed at 2 weeks

On the treated side no significant difference in MGT was seen between the different experimental groups but the values showed a distinct tendency

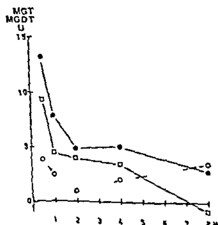


Fig 35 Growing animals Mean growth value (MGT) and growth difference value (MGDT) in each e perimental group at observation times of 3 days to 8 weeks ●—● MGT for treated tibia ○—○ MGT for control tibia □—□ MGDT

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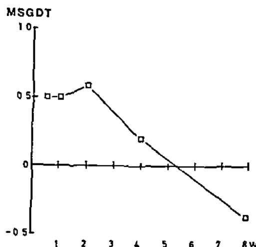


Fig 33 Growing animals Mean standardized growth difference value (MSGDT) in each experimental group at observation times of 3 days to 8 weeks

at time point 2 8 MAD was 0 6, which is an almost significant difference value

A study of the relations of the individual experimental groups showed that on the control side MAT was 0 4 at an observation time of 3 days 0 05 at 2 weeks, 0 at 4 weeks and 0 08 at 8 weeks (Fig 32) The decrease between the observation times of 3 days and 2 weeks was not significant On the treated side MAT was 0 5 at an observation time of 3 days, 0 9 at 2 weeks, 0 35 at 4 weeks and 0 43 at 8 weeks The increase from 0 5 to 0 9 is not significant The decrease from 0 9 to 0 35 is almost significant There was a highly significant positive activity difference at an observation time of 2 weeks

Studies of the Standardized Growth Difference

Growing animals (Fig 33)

At observation times of 3 days and 1 week almost significant positive *MSGDT* values were found and at 2 weeks, highly significant positive MSGDT values An almost significant positive difference in MSGDT was found between the combined animal groups observed at 3 days 1 week and 2 weeks compared with the groups observed at 4 and 8 weeks

Adult animals (Fig 34)

Almost significant positive MSGDT values were found in the animal group observed at 1 week and highly significant at 2 weeks The group observed at 2 weeks showed a significantly higher MSGDT than the group observed at 3 days and an almost significantly higher value than the group observed at 4 weeks

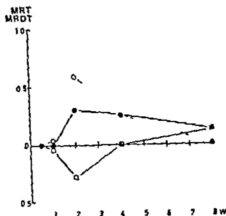


Fig 37 Growing animals Mean resorption value (MRT) and resorption difference value (MRDT) in each experimental group at observation times of 3 days to 8 weeks ●—● MRT for treated tibia ○—○ MRT for control tibia, □—□ MRDT

during different periods of observation has been assessed Their observations have been combined with studies of the morphology of the bone at the end of each observation period and from these findings conclusions have been drawn on the course of the periosteal bone growth

In the present investigation this course has been studied by other methods as follows

(1) Qualitative recording of the bone formation capacity of the periosteum some days before the angiographic examination was performed by determining the activity values The development of the activity values during the whole period of observation eight weeks was studied by means of regression analysis

(2) Quantitative recording of the bone formation was performed by measuring the thickness of the bone and osteoid tissue which had formed during the last days of each observation period The large variation in the bone formation rate between different animals and different sectors was evened out by calculating the standardized growth difference For this purpose the quantitative measurement value was converted to a qualitative unit

(3) A recording was made of whether the sectors showed superficial resorption or not

By studying these variables for the treated side for the control side and for the difference between the treated and control sides the development of the subperiosteal bone formation activity could be assessed both qualitatively and quantitatively

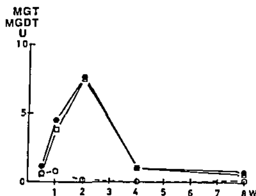


Fig 36 Adult animals Mean growth value (MGT) and growth difference value (MGDT) in each experimental group at observation times of 3 days to 8 weeks ●—● MGT for treated tibia ○—○ MGT for control tibia □—□ MGDT

towards lower values at longer observation times There was an almost significant MGDT between the treated and control side at observation times of 1 and 2 weeks The highest MGDT was found at 3 days but this value was not significantly increased The value is largely accounted for by a high GD in 8 pairs of sectors in the three animals *125*, *3* and *81*

Adult animals (Fig 36)

On the control side MGT was 0 6 U at an observation time of 3 days 0 1 at 2 weeks 0 at 4 weeks and 0 1 at 8 weeks On the treated side this value was 1 1 U at 3 days 7 6 at 2 weeks 1 0 at 4 weeks and 0 7 at 8 weeks The maximal MGT on the treated side and the maximal MGDT were found at an observation time of 2 weeks At this time MGDT was almost significant

Study of the Resorption Values (Fig 37)

A significantly positive MRT was found both on the treated side and on the control side at an observation time of 2 weeks MRT was so much higher on the control side than on the treated side that at this observation time MRDT was almost significantly negative At observation times of 3 days and 1 4 and 8 weeks MRDT was not significant

Discussion

In previous studies on the reaction of the periosteum after disturbances of the endosteal circulation (Rohlich 1941 Kuntscher 1957 Flatmark 1967 Trueta & Cavadias 1955 Richany *et al* 1965 Mital & Cohen 1966 Zucman *et al* 1968) the total amount of bone which has newly formed

than the absolute growth on the control side at 3 days (3 8 U) a significant absolute growth difference was found at 2 weeks

The study of sectors undergoing resorption (MRT) showed that a significantly increased number of sectors were undergoing resorption at an observation time of 2 weeks both on the treated and control side The resorption was so much greater on the control side that an almost significant negative resorption difference (MRDT) was found at 2 weeks The analysis thus showed that the bone formation activity both on the treated and on the control side at an observation time of 2 weeks was distinctly lower than at 3 days In growing animals the periosteum on the treated side thus seems to be activated to bone formation most strongly on the days immediately following reaming of the medullary cavity — no distinct maximum was recorded The difference between the treated and the control sides was greatest at an observation time of 2 weeks This rapid increase in the periosteal bone formation following medullary trauma corresponds well with the results of Tonna & Cronkite (1961) They studied the DNA synthesis in the osteogenic layer of the tubular bone after fracture and found that away from the fracture this began to increase 16 hours after the fracture and reached a maximum at 32 hours In the present material a later phase in the bone formation was studied than in the material reported by Tonna & Cronkite

At an observation time of 4 weeks a partial elimination of the activity difference the standardized growth difference the absolute growth difference and the resorption difference took place in the growing animals At an observation time of 8 weeks a tendency was observed to more active bone formation on the control side than on the treated side

Adult Animals

As in the growing animals the control side in the adult rabbits showed its maximal activity value (MAT) at an observation time of 3 days In spite of this relatively high activity value only a very small absolute growth value (MGT) was found The activity value on the control side then decreased and reached a minimum at 2–4 weeks The activity value (MAT) and absolute growth value (MGT) on the treated side the activity difference (MADT) the standardized growth difference (MSGDT) and the absolute growth difference (MGDT) all increased to a maximum at an observation time of about 2 weeks As in the growing animals there seemed to be a partial elimination of the differences between the treated and control sides at 4 weeks No compensatory phase with greater bone formation activity on the control side than on the treated side was observed in the adult animals

In the growing animals all sectors were active both on the treated and the control side (*MAT* = *1*) *at an observation time of 3 days* *Since all animals* in this group were given tetracycline 1 day after the operation, these activity values actually reflect the situation about 1 day postoperatively The high activity which was observed at that time on the control side may either reflect the normal bone formation activity of the animal or be a result of stimulation from the operation on the contralateral bone The results obtained by Tonna & Cronkite (1961) appear to contradict the second possibility On study of the cell proliferation in the periosteum after experimental fracture on the rat tibia, they found no stimulation of the cell division on the contralateral bone

The high activity value on the control side meant that no activity difference occurred at an observation time of 3 days despite the fact that the activity value on the treated side was then maximal At 3 days the absolute growth on the treated side (MGT) and the absolute growth difference (MGDT) showed their highest values But at that time point the increase in MGDT was not significant since it referred to a relatively small number of sectors which showed a very high degree of growth The standardized *growth difference (MSGDT) was almost significantly increased* however, at an observation time of 3 days This indicates that a difference existed between the growth on the treated side and on the control side at this time point even though this was not expressed in an activity difference or an absolute growth difference

Compared with the animals observed at 3 days those observed at 2 weeks *showed a lower activity value (MAT) and a lower absolute growth* value (MGT) on the treated side The absolute growth difference (MGDT) was also smaller at 2 weeks while the standardized growth difference (MSGDT) was not significantly changed The activity difference (MADT) the standardized growth difference (MSGDT) and the absolute growth difference (MGDT) showed almost significantly positive values however at an observation time of 2 weeks *The high activity difference (MADT) which was* found at that time point was due to a large reduction of the activity value (MAT) on the control side and the significant activity difference occurred despite the fact that the activity value on the treated side was lower then than that at 3 days Also for the occurrence of the significant positive absolute growth difference (MGDT) at an observation time of 2 weeks a significant reduction of *the absolute growth (MGT) on the control side* played a decisive role Even though the absolute growth on the treated side at an observation time of 2 weeks was thus only slightly greater (4 8 U)



Fig 38 Histological cross section of dorsal part of cortex observation time 2 weeks Growing animal 45 Stained osteocytic nuclei are present in the inner avascular part of the cortex

Shrinkage of the osteocytic nucleus was seen in bone tissue also on the control side and could not therefore be used as a sign of bone necrosis

In sections from animals observed at 3 days small scattered areas were observed in the inner and middle part of the cortex where the osteocytic lacunae lacked stainable material while in other parts of the cortex and in the surrounding soft tissues the nuclear staining was good No difference between the treated and the control side was observed however

Sections from animals observed at 1 week showed similar pictures to those from animals observed at 3 days

In sections from animals observed at 2 weeks scattered areas larger than on the control side were seen in the middle and inner parts of the cortex with practically no stainable osteocytic nuclei on the treated side These areas sometimes comprised more than one quarter of the surface area of the section In sections from one animal (45) the vessels in the middle and inner parts of the cortex showed no filling with Indian ink In these areas however several stained osteocytic nuclei were seen (Fig 38) In a few bone fragments which lay freely in the medullary cavity which completely lacked Indian ink filled vessels stained nuclei were observed in several osteocytic

Conclusion

In growing animals the bone formation activity on the treated side seemed to be greatest on the days immediately after reaming of the medullary cavity This activity then decreased on the treated side so that at 2 weeks it was on the same level as that on the control side at 3 days Since, however, the reduction of the bone formation activity was at the same time relatively greater on the control side there was still a significant difference between the treated and control sides at 2 weeks At an observation time of 4 weeks the bone formation difference was almost eliminated and at 8 weeks there was *a tendency to a negative difference*

In adult animals there was somewhat greater bone formation activity on the treated side than on the control side at an observation time of 3 days This difference was maximal at about 2 weeks and was partly eliminated at 4 weeks

STUDY OF THE HISTOLOGICAL SECTIONS

The histological picture in periosteal bone formation the reconstruction of the cortex and the reformation of the structure of the medullary cavity after disturbances of the endosteal circulation have been described in detail previously in histological studies by Axhausen & Bergmann (1937) Ham & Harris (1956) and Branemark (1964) among others In the present study the interest was therefore focused on the extent of the cortical necrosis The appearance and stainability of the osteocytic nuclei were thus correlated to the Indian ink filling of the intracortical vessels in the area

Method

The histological sections were stained with haematoxylin and eosin The Indian ink filling of the intracortical vessels was assessed both on the histological and the angiographic sections prepared from the same paraffin embedded material

Results

The osteocytic nuclei could best be studied on the histological cross sections From each main experimental group at observation times of 3 days up to and including 4 weeks sections were obtained from at least one animal in which the nuclear staining was satisfactory The examination was therefore concentrated on these sections In sections from several other animals however there was no nuclear staining at all either in the cortex or in the surrounding soft tissues



Fig 38 Histological cross section of dorsal part of cortex observation time 2 weeks Growing animal 45 Stained osteocytic nuclei are present in the inner avascular part of the cortex

Shrinkage of the osteocytic nucleus was seen in bone tissue also on the control side and could not therefore be used as a sign of bone necrosis

In sections from animals observed at 3 days small scattered areas were observed in the inner and middle part of the cortex where the osteocytic lacunae lacked stainable material while in other parts of the cortex and in the surrounding soft tissues the nuclear staining was good No difference between the treated and the control side was observed however

Sections from animals observed at 1 week showed similar pictures to those from animals observed at 3 days

In sections from animals observed at 2 weeks scattered areas larger than on the control side were seen in the middle and inner parts of the cortex with practically no stainable osteocytic nuclei on the treated side These areas sometimes comprised more than one-quarter of the surface area of the section In sections from one animal (45) the vessels in the middle and inner parts of the cortex showed no filling with Indian ink In these areas however several stained osteocytic nuclei were seen (Fig 38) In a few bone fragments which lay freely in the medullary cavity which completely lacked Indian ink filled vessels stained nuclei were observed in several osteocytic



Fig 39 Hematoxylin eosin stained histological section observation time 2 weeks Growing animal 45 A fragment of cortical bone is lying freely in the medullary cavity In the surrounding area there are no newly formed blood vessels Stained nuclear material is seen in several of the osteocytic lacunae

lacunae (Fig 39) On fluorescence microscopy of the adjacent sections it was found that the bone fragments in the medullary cavity did not fluoresce

In sections from the treated side of animals observed at 4 weeks, scattered areas larger than those observed at 2 weeks were sometimes found in the middle and inner parts of the cortex where most of the osteocytic lacunae lacked stainable nuclei Corresponding angiography showed that some of the vessels here were filled with Indian ink In the cortex no sharp boundary was seen between the areas without and those with nuclear staining Nearest to the medullary cavity nucleus bearing osteocytic lacunae were observed where no Indian ink-filled vessels were seen

Discussion

Necrosis occurs in cortical bone a short time after the circulation to the cortex has been arrested (see literature reference p 21) The first histological sign of bone necrosis is shrinking of the osteocytic nucleus The necrotic nucleus becomes fragmented and nuclear material is carried away when the

fluid circulation to the area has been restored (Axhausen & Bergmann 1937) In certain cases this can take place only a few days after the occurrence of the necrosis but in other cases it can take a very long time The shrinking of the osteocytic nucleus in necrosis has been utilized by many investigators in the diagnosis of bone necrosis In the present material however the preparatory procedure gave rise as a rule to shrinkage of the osteocytic nucleus even in bone tissue which was not necrotic It was therefore not possible to determine the extent of the bone necrosis from the shrinkage of the osteocytic nuclei Instead an attempt at such determination was made by observing whether or not the osteocytic lacuna contained stainable nuclear material The absence of such material is usually a definite sign that the bone is necrotic (Axhausen & Bergmann 1937) but falsely empty osteocytic lacunae can occur in that the nucleus does not occupy the whole lacuna and that the section cuts through the lacuna without encountering the nucleus

In the specimens from this series of experiments there was no sharp borderline between nucleus bearing and non nucleus bearing regions of the cortex The latter regions visible at 2 weeks and increasing with observation time were observed especially on the treated side and there within the inner and middle part of the cortex Often however stainable nuclear material remained in the cortex even just adjacent to the medullary cavity at least up to 4 weeks after the reaming in the area where angiography showed that no vessels were filled with Indian ink

In loose bone fragments in the medullary cavity stainable nuclear material was observed 2 weeks after the reaming of the medullary cavity Corresponding fluorescence specimens showed that the bone fragments in the medullary cavity were not fluorescent which provided that no vessels were seen in the medullary cavity can be regarded as a sign that no fluid diffusion to the area had taken place two days before angiography

Thus stainability of osteocytic nuclei by no means constitutes a guarantee of the absence of necrosis even 4 weeks after operation

In the present material the extent of the bone necrosis could thus not be determined by the histological method used within 4 weeks after the operation This seems to be due to the fact that all necrotic nuclear material has not then been transported away from the osteocytic lacunae

It would seem therefore that the extent of the cortical damage after reaming of the medullary cavity can better be evaluated from the angiographic findings in specimens with a short observation time than from a study of the histological picture

Marrow Embolism as a Cause of Intracortical Circulation Block after Surgery of the Medullary Cavity

On reaming of the medullary cavity the intracortical circulation in the diaphysis is disturbed This has been demonstrated by Indian ink angiography and is discussed on page 74 The blood vessels do not fill with Indian ink within large areas the extent of which varies greatly between different animals and between different sectors in the same animal The reason for the deficient filling with Indian ink would therefore seem to be not only the elimination of the medullary circulation but also a simultaneous direct effect on the intracortical blood vessels One possible cause of the intracortical circulatory disturbance is that the Haversian canals are occluded by medullary cavity contents which are squeezed into the canals when a surgical operation is performed in the medullary cavity

In man fat emboli in the lungs often occur after fracture of the long tubular bones (for literature see Bergentz 1961) Kjerstell (1969) has shown that pulmonary fat emboli occurring in experimental femoral fractures in the dog originate in the traumatized fat tissue especially in the medullary cavity Stained fat which is injected into the medullary cavity of a tubular bone gives rise to multiple emboli in the lungs when the bone is fractured (Glas *et al* 1956) but also without fracture if the contents of the medullary cavity are mobilized by the introduction into it of a steel wire (Busch 1866) Bisgard & Baker (1940) claim that medullary fat enters the circulatory system for the reason that on such trauma the fat is released from the fat cell and becomes fluid that it accumulates under pressure on bleeding in the medullary cavity and that the open veins through the cortex do not collapse

Bone marrow can thus leave the medullary cavity on intramedullary trauma but no investigations on the pathway of the marrow from the medullary cavity through the cortex and its possible influence on the intracortical circulation appear to have been reported previously A series of experiments was thus carried out with the aim of answering the following questions

1 Do different degrees of medullary trauma give rise to different degrees of influence on the intracortical circulation?

Table 8 *Observation time number of animals and kind of treatment in the animal group used for study of fat emboli in the intracortical canals*

Observation time	No of animals	Treated tibias		
		Suction	Reaming	Brushing
1 day	13	5	5	5
1 week	1		1	1
2 weeks	3		2	3
4 weeks	3		2	3

2 Are medullary emboli the cause of the disturbance of the intracortical circulation?

Material

The material comprised 27 growing and adult non pregnant rabbits of both sexes Five of these animals (Table 9) which also served as controls were taken from the material presented in Table 1 namely 109 114 123 124 and 125 all of which belonged to the group studied at an ob ervation time of 3 days The sizes of the other animal groups the lengths of the obser vation times and the kind of treatment are given in Table 8 Two animals died during the operation

Methods

The anaesthesia and operation were performed as described in chapter 2

The medullary cavity of the tibia was evacuated by one of the following three methods which gave rise to different pressure increases in the medullary cavity and partly as a result of these pressure increases was considered to be exposed to different degrees of medullary trauma (see p 40) (1) suction (2) reaming (3) brushing

Groups of anim ls were studied after observation times of 1 day and 1 2 and 4 weeks (Table 8) The circulatory system was filled with Indian ink as described in chapter ? In a deep frozen state the tibia was divided 2 5 and 7 5 cm from the tibio talar joint From e ch end of the middle part which was decalcified 1 cm was sawn off and used for Spalteholz preparations from which a drawing was made with the va cular front outlined according the method described previously (see p 29) On these drawings the percentage proportion of the cortical cross section with no Indian ink filling of the vascular system was calculated and named avascular cortex From the intermediate part of the diaphysis 10–15 μ thick frozen se tions were prepared The section were stained with Sudan 3 and haematoxylin and then mounted under a co er gla s with Permount Since the contents of the medullary cavity in the tibial diaphysis in the rabbit consist to a large part of fat, fat staining with Sudan 3 was used to indi ate the presence of bone marrow

From the f e animals from the material presented in Table 1 bone material for frozen-sect oning was taken from the distal part of the diaphysis.

Table 9 *Mean number of marrow emboli per section from control and reamed tibias and the percentage of avascular cortex in the 5 animals from Table 1*

Animal no	Fat emboli per section		Percentage avascular cortex
	Control	Reamed	
109	0 3	2 0	19
114	0 3	3 7	26
123	0 7	20 0	61
124	0 0	2 3	9
125	0 7	8 0	31
Mean	0 5	7 2	

Results

Both tibiae from the five animals from Table 1 were studied three Sudan stained histological sections being studied from each tibia In each section from the untreated control tibia an average of 0 5 fat emboli were found in intracortical vessels The range of variation was 0–1 fat droplet per section In sections from the reamed tibia an average of 7 2 fat droplets per section were found The results are presented in Table 9 The table shows that the larger the amount of avascular cortex on the treated side the greater the number of fat droplets in the intracortical canals on that side

Result of Differentiated Medullary Trauma

The percentage of avascular cortex 1 day after operation can be seen in Table 10 The table shows that reaming of the medullary cavity gave somewhat greater intracortical vascular damage than suction of the contents of the medullary cavity both in the distal and the proximal part of the diaphysis The difference was not significant Brushing out of the contents of the medullary cavity gave somewhat greater vascular damage than reaming or suction of the contents The difference in this respect in the distal sections was significant at the 10 per cent level A study of the Sudan stained sections showed that Sudan stained material was present in many Haversian canals in the areas of the cortex that lacked Indian ink-filled vessels (Color pl 3 *b c*) As a rule the Sudan-stained material obliterated the entire Haversian canal, which then did not fill with Indian ink In some cases only small fat droplets were found in the canals and Indian ink filled blood vessels passed these droplets This was rather unusual however, and seemed to occur only in the outer part of the cortex In these cases there were possibly two blood vessels in the same Haversian canal of which one was obliterated by fat Haversian canals which were obliterated by fat were observed in

Table 10 *Mean weights mean values and ranges of variation of avascular cortex for the tibias of each group of 5 rabbits 1 day after suction reaming or brushing of the medullary cavity*

P indicates the proximal section taken about 5 7 cm above the tibiotalar joint and *D* the distal section from about 2 7 cm above the same joint

		Suction	Reaming	Brushing
Percentage	P	44 (8–61)	56 (23–77)	64 (46–85)
avascular cortex	D	23 (6–34)	37 (14–54)	81 (64–93)
Mean weight kg		3 5 (3 3–3 9)	3 4 (3 1–3 9)	3 3 (3 1–3 7)

greatest abundance close to the medullary cavity In animals in which angiography preparations showed avascularity of the outer parts of the cortex Sudan stained material in Haversian canals was also observed however in the outer part of the cortex In some preparations especially from the fibular part of the proximal area of the diaphysis a layer of marrow up to some mm thick was seen under the periosteum (Color pl 3 *d*)

In preparations from animals studied at observation times of 1 and 2 weeks the same pattern of fat in the Haversian canals was found as at an observation time of 1 day At an observation time of 4 weeks some of the canals which contained Indian ink filled vessels were wider than those observed at 2 weeks In some cases (Color pl 3 *f*) it was found that a Haversian canal had increased in calibre but that fat was still present in the canal at the side of an Indian ink filled blood vessel Color pl 3 *e* shows how a cutter head is revascularizing an osteone whose canal in front of the cutter head is obliterated by fat

Two of the animals died during brushing out of the medullary contents They showed cyanosis tachypnoea and tachycardia followed by bradycardia and died despite artifical respiration At autopsy fat emboli were observed in Haversian canals of the treated tibia in many pulmonary vessels and in one renal vessel

Discussion

The normal occurrence of fat in cortical bone was studied by Conklin *et al* (1956) They found only small quantities of lipids in osteocytes osteocyte lacunae canaliculi and in organic matrix and no fat droplets in the Haversian canals Jones *et al* (1965) found in two patients with idiopathic avascular necrosis of the femoral head multiple fat droplets in the subchondral arterioles and in the capillaries in the necrotic bone Karlstrom *et al* (1939) considered that one cause of avascular bone necrosis might be fat emboli in the intracortical blood vessels

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CHAPTER 5

Periosteal New Bone Formation Correlated to Endosteal Bone Removed, Cortical Vascular Damage and Subperiosteally Squeezed out Bone Marrow

There would seem to be several causative factors in periosteal new bone formation Phemister (1930) Axhausen & Bergmann (1937) and Trueta (1963) consider that vascularly disturbed cortical bone causes local stimulation of periosteal osteogenic cells to new bone formation Frost (1963) and Schenk (1967) claim that mechanical factors contribute to stimulation of the periosteum Zucman *et al* (1968) have shown that bone marrow which after an operation in the medullary cavity has become localized subperiosteally has a strong stimulatory effect on bone formation The high osteogenetic potency of bone marrow has been demonstrated previously by several investigators including Urist & McLean (1952) and Burwell (1964) especially in connection with transplantation experiments

The experimental methods used in the present study give prerequisites for new bone formation according to all of the above possibilities In this chapter studies are described on the relationship between avascular bone or bone removed on reaming and the amount of new bone formed subperiosteally The effect of subperiosteally localized bone marrow must however be evaluated indirectly

For the studies of this relationship statistical methods of analysis were used

Material

Twenty four albino male and non pregnant female growing rabbits were used The ages of the animals were stated by the breeder to be between 14 and 18 weeks They were divided into two groups 1 and 2 Three animals were excluded from group 1 owing to fracture of the treated tibia and 4 animals were excluded from group 2 because of death in connection with the operation After these exclusions group 1 comprised 7 animals and group 2 10 animals The mean weight of group 1 was 2340 g with a range of variation of 1600 2850 g and of group 2 2470 g range 1700-2650 g

This series of experiments showed that when the contents of the medullary cavity were removed by different methods, which gave rise to different degrees of medullary trauma, varying degrees of vascular damage were obtained in the diaphyseal cortex lying outside. Suction of the contents of the medullary cavity gave the least vascular damage, while brushing out of the contents, which caused the largest increase in the intramedullary pressure, gave the greatest vascular damage. In those areas of the cortex in which the blood vessels did not fill with Indian ink at angiography, an abundance of Sudan stained droplets was often found in the Haversian canals. Sudan staining demonstrates the presence of fat and was used to indicate medullary tissue. In the areas in which almost every blood vessel filled with Indian ink, no or only a very small number of fat droplets were observed in the Haversian canals. In no section from control tibias, which were not operated on, was more than one Haversian canal obliterated by fat. The fat in the control tibias may have constituted emboli from the other treated tibia. On the histological sections it could not be determined whether the fat lay inside or outside the blood vessels. In preparations studied at an observation time of 4 weeks it was found that fat was still present in the Haversian canals and that it offered resistance to revascularization of the bone. Jones & Sakovich (1966) injected Lipiodol intravenously in the rabbit and observed Lipiodol in intracortical vessels during an observation time of 5 weeks. Cohen & Harris (1958) reported that the canals in cortical bone were wider nearer to the medullary cavity than peripherally under the periosteum. This could contribute to the fact that fat droplets on their way from the medullary cavity were stopped in the Haversian canals.

The rather high mean percentage of avascular cortex in the suctioned group may depend on the fact that high pressure was produced in the medullary cavity in some animals by the awl.

Conclusion

Intracortical emboli of the bone marrow are thus an important cause of intracortical vascular damage after medullary trauma. The contents of the medullary cavity can be squeezed out subperiosteally where they can be observed macroscopically as a haemorrhage.

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The experimental methods used in the present study give prerequisites for new bone formation according to all of the above possibilities In this chapter studies are described on the relationship between avascular bone or bone removed on reaming and the amount of new bone formed subperiosteally The effect of subperiosteally localized bone marrow must however be evaluated *indirectly*

For the studies of this relationship statistical methods of analysis were used

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Methods

The anaesthesia and operation were performed as described in chapter 2 In group 1 the medullary cavity of the left tibia was evacuated by reaming and that of the right tibia by suction In group 2 the medullary cavity of the left tibia was evacuated by brushing and that of the right tibia by suction For both groups of animals the left tibia was called the treated tibia and the right the control tibia

Bone Labelling

The animals were given approximately 50 mg tetracycline/kg body weight intraperitoneally on the day of operation and 5 days postoperatively

Angiography

Angiography was performed as described in chapter 2 7 days after the operation

Preparation of the Sections for Analysis

After fixation in formalin the tibia was divided in the deep frozen state 2 5 cm above the tibiotalar joint From the distal part of the proximal fragment three consecutive 1 2 cm long preparations were sawn These were named from the distal end preparations *a* *b* and *c* Preparations *a* and *c* were embedded in methyl metacrylate and preparation *b* was decalcified and embedded in paraffin From the distal and proximal parts of preparation *a* and from the distal part of preparation *c* $^1/_2$ mm thick slices were sawn and used for the preparation of ground sections for fluorescence microscopy Further $^1/_2$ mm thick slices were then sawn from the same areas and used for Spalteholz preparations after removal of the methyl metacrylate with chloroform and decalcification of the specimen (See description of methods on p 29) In this way three pairs of preparations were obtained Each pair comprised one fluorescence preparation and one Spalteholz preparation taken from immediately adjacent bone The pairs of preparations were named from the distal end section 1 (SN1) section 2 (SN2) and section 3 (SN3) All three sections together were called SNT SN1 was thus obtained from the distal part of preparation *a* SN2 from the proximal part of preparation *a* and SN3 from the distal part of preparation *c* The distance between SN1 and SN2 was about 11 mm and between SN2 and SN3 about 14 mm From each section an image drawing was made in the way described on p 28 Each image drawing was divided into four sectors and each sector into the areas AB CD CE and DE after which the sizes of these areas were calculated Area AB in sector 1 was called AB1 in sector 2 AB 2 and so on

Corresponding designations were used to denote the localization of the areas CD CE and DE

Analytical Methods

Between the values obtained for corresponding AB CD CE and DE areas on the treated and control sides the difference the quotient and the difference between the logarithms were calculated Analysis showed that difference calculation gave better correlation between the different sections than calculation of the quotient or of the difference between the logarithms Difference calculation was therefore used throughout The differences between the areas were denoted ABd CDd CEd and DEd The values obtained were expressed in mm

By for example the abbreviation CDd2SN3 is thus meant the difference between the sizes of areas CD on the treated and control sides in sector 2 in section 3

Calculations of the mean values of ABd CDd CEd and DEd were performed separately for the groups of animals treated by reaming (group 1) and by brushing (group 2) (Table 11) For groups 1 and 2 together each ABd value was correlated with the ABd values of all other sectors and certain formed sums of sectors (Table 12) By simple correlation analysis (Table 13) and by multiple regression analysis (Table 14) the ABd values were correlated with the corresponding values for CDd and DEd

Results

General Reaction of the Animals

In no case did wound infection or wound rupture occur The mean change in weight during the experimental period of 1 week was −52 g in group 1 with a range of variation of +8 to −197 g and −34 g in group 2 with a range of variation of +310 to −300 g

The animals bore weight normally on both legs a few days after the operation

Mean Value Calculation of ABd CDd DEd and DEd (Table 11)

Calculation of the mean value of each sector in the three sections was performed separately for the reamed and brushed groups of animals The mean ABd value was positive in all sectors in both the reamed and brushed groups and reached the almost significant level in sectors 1 and 2 in the reamed and in sector 2 in the brushed animals The mean ABd value was somewhat higher throughout in the brushed animals than in the reamed but this difference did not reach the level of significance

The mean CDd value was highly significantly raised in all sectors in the brushed animals In the reamed animals the mean CDd value was highly significantly raised in sectors 1 and 3 and almost significantly raised in sectors 2 and 4

On comparing the mean CDd values for the reamed and brushed animals it was found that these were higher throughout in the latter The difference was almost significant in sectors 2 and 4 but not significant in the other sectors

The mean CEd value was highly significantly increased in all sectors in both the reamed and brushed animals In sectors 2 and 4 in which most bone had been removed on reaming the mean CEd value was somewhat higher in the reamed than in the brushed animals but in the other sectors somewhat lower The difference between the reamed and brushed groups did not reach the level of significance

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Between the values obtained for corresponding AB CD CE and DE areas on the treated and control sides the difference the quotient and the difference between the logarithms were calculated Analysis showed that difference calculation gave better correlation between the different sections than calculation of the quotient or of the difference between the logarithms Difference calculation was therefore used throughout The differences between the areas were denoted ABd CDd CEd and DEd The values obtained were expressed in mm²

Table 12 *The correlation coefficient (r) between the ABd values in individual sectors and certain sums of sectors*

The following significance limits (taken from *Documenta Geigy* 6th edn p 61) were used with 15 degrees of freedom $|r| \leq 0.48$ not significant $0.48 < |r| < 0.61$ almost significant $0.61 < |r| < 0.73$ significant $|r| \leq 0.73$ highly significant. These limits hold stringently under certain idealized condition

Sectors	No	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
ABd1 SN1	1																		
ABd1 SN	2	0.95																	
ABd1 SN3	3	0.85	0.94																
ABd1 SNT	4	0.94	0.99	0.98															
ABd2 SN1	5	0.85	0.82	0.72	0.80														
ABd2 SN2	6	0.68	0.63	0.53	0.61	0.92													
ABd2 SN3	7	−0.22	−0.07	0.12	0.01	0.19	0.16												
ABd2 SNT	8	[illegible]	[illegible]	0.61	0.59	0.68	0.72	0.56											
ABd3 SN1	9	0.80	0.75	0.61	0.72	0.93	0.86	−0.13	0.67										
ABd3 SN2	10	0.38	0.27	0.11	0.22	0.65	0.74	−0.07	0.55	0.80									
ABd3 SN3	11	0.91	0.92	0.84	0.90	0.72	0.54	0.02	0.54	0.72	0.38								
ABd3 SNT	12	0.82	0.74	0.60	0.71	0.83	0.75	−0.02	0.65	0.92	0.79	0.85							
ABd4 SN1	13	0.74	0.67	0.53	0.64	0.89	0.85	−0.13	0.65	0.99	0.86	0.67	0.91						
ABd4 SN2	14	0.49	0.36	[illegible]	0.37	0.57	0.68	0.00	0.54	0.68	0.79	0.52	0.76	0.67					
ABd4 SN3	15	0.83	0.80	0.74	0.83	0.60	0.42	0.18	0.56	0.63	0.37	0.96	0.84	0.59	0.51				
ABd4 SNT	16	0.72	0.64	0.49	0.61	0.79	0.75	0.03	0.67	0.91	0.87	0.77	0.99	0.92	0.79	0.77			
ΣABdSn1 + 2 + 3	17	0.89	0.87	0.79	0.86	0.89	0.79	0.09	0.77	0.91	0.66	0.91	0.95	0.88	0.68	0.87	0.92		
ΣABdSN3	18	0.81	0.88	0.90	0.90	0.65	0.47	0.34	0.71	[illegible]	[illegible]	0.93	0.74	0.56	0.43	0.93	0.67	0.87	
ΣABdSN1 + 2	19	0.80	[illegible]	0.57	0.68	0.92	0.90	−0.12	0.69	0.98	0.95	0.74	0.96	0.98	0.76	0.67	0.95	0.93	0.62

Table 11 *Mean values ($\bar{X}$ in square mm) and standard errors (S E) for ABd CDd CEd and DEd in sectors 1 to 4 for all sections in the reamed and brushed groups and the difference values between the groups*

The degree of significance is denoted by asterisks

	Reamed		Brushed		
Sector	$\bar{X}_R$	±S E	$\bar{X}_B$	±S E	$\bar{X}_R - \bar{X}_B$
ABd1 SNT	0 12*	0 03	0 39	0 28	−0 17
ABd2 SNT	0 26*	0 09	0 27*	0 11	−0 01
ABd3 SNT	0 24	0 28	0 30	0 18	−0 06
ABd4 SNT	0 19	0 20	0 20	0 11	−0 01
CDd1 SNT	1 53***	0 26	2 16***	0 36	−0 63
CDd2 SNT	0 61*	0 20	1 51***	0 23	−0 90*
CDd3 SNT	1 10***	0 13	1 65***	0 35	−0 55
CDd4 SNT	0 62*	0 21	1 39***	0 20	−0 76*
CEd1 SNT	1 88***	0 21	2.16***	0 36	−0 29
CEd2 SNT	1 63***	0 20	1 51***	0 23	+0 12
CEd3 SNT	1 26***	0 19	1 65***	0 35	−0 39
CEd4 SNT	1 55***	0 21	1 40***	0 20	+0 16
DEd1 SNT	0 35**	0 06			
DEd2 SNT	1 02***	0 10			
DEd3 SNT	0 16	0 07			
DEd4 SNT	0 93***	0 06			

The mean DEd value calculated in the reamed group of animals was highly significantly increased in sectors 2 and 4 and significantly increased in sector 1

Calculation of Correlation between ABd Values in Individual Sectors and Certain Sums of Sectors (Table 12)

The three sections in sector 1 were all highly significantly correlated to each other In sector 2 section 3 differed greatly from the other two sections In sector 3 section 2 differed greatly from section 3

Sector 1 was the most homogeneous sector The three sections in this sector were therefore suitable for use as reference sections All three sections in sector 1 showed a weak correlation not only with ABd2SN3 which was very weakly correlated to all other sectors and sums of sectors but also with ABd3SN2 and ABd4SN2 ABd3SN2 and ABd4SN2 were highly significantly correlated with each other

Almost all other sectors and sums of sectors were highly significantly or almost significantly correlated with each other

Table 14 *Regressors with coefficients significantly different from 0 and coefficients of determination* (R^2) *in an analysis with the sizes of ABd areas of different locali ations as dependent variable and similarly locali ed CDd and DEd areas and also the type of operation as independent variables*

Reamed = 1 Brushed = 0 n = 17

Dependent variable	Regressors with significance according to multiple regression analysis	R^2
ΣABd in		
SN1	DEd (neg)	0 43
SN2	None	0 30
SN3	None	0 45
SN1 + 2	None	0 23
SN1 + 2 + 3	None	0 19
Sector 1	None	0 20
2	None	0 23
3	None	0 18
4	DEd (neg) Reamed (pos)	0 47

An almost significant positive correlation was found between ABd and the type of operation in sector 4 This correlation was found at DEd = 0 but not at those values for DEd which were obtained for the reamed animals This almost significant correlation therefore lacked conclusive value

Discussion

When the bone marrow in the rabbit tibia was removed by reaming or by brushing greater intracortical vascular damage and somewhat greater periosteal new bone formation occurred than when the contents were removed by suction With all three types of operation the medullary circulation was completely destroyed in the diaphysis of the bone It would seem therefore that factors other than the loss of the medullary circulation should constitute the reason for the fact that somewhat more bone was formed subperiosteally on reaming or brushing than on suction

In the studies described in chapter 4 it was shown that the intracortical vascular damage was due essentially to the fact that the intracortical blood vessels were obliterated by bone marrow which had been forced *in as a result* of the increase in pressure in the medullary cavity during the operation

Correlation analysis and multiple regression analysis of the relationships between the ABd values and the corresponding *CDd and DEd* values showed that the amount of avascular bone in and the amount of bone removed on reaming from the underlying cortex had no apparent explana

Table 13 *The correlation coefficient (r) between the dependent variable ABd and the corresponding independent variables CDd and DEd for all individual sections and sectors in the 17 animals*

For the evaluation of significance see Table 12

	Correlation	
	ABd/CDd	ABd/DEd
SN1	0 09	0 08
SN2	0 16	0 29
SN3	0 63*	0 45
Sector 1	0 42	−0 16
2	0 39	−0 07
3	0 27	−0 24
4	0 05	−0 15

Correlation between Dependent Variable ABd and Corresponding Independent Variables CDd and DEd (Table 13)

A correlation analysis was performed both for the sum of all sectors in each individual section and for the sum of each individual sector with the same localization in all three sections

The correlation between the ABd values and the CDd values were positive throughout An almost significant value was attained in section 3 This could be explained by the fact that one animal differed greatly from the rest and the significance was therefore of no explanatory value

The correlations between the ABd and DEd values were positive throughout for individual sections, but negative throughout for individual sectors The values did not reach the level of significance

Regression Analysis with the Size of Differently Localized ABd Areas as Dependent Variable and the Size of Similarly Localized CDd and DEd Areas and also the Type of Operation as Independent Variables (Table 14)

The total explanatory value expressed as R was low throughout for the variables studied, the maximal value being 0 47

On regression analysis an almost significant negative relationship was found between ABd and DEd in section 1 and in sector 4 On closer analysis of these relationships it was found however that they could be explained by the fact that the results from one animal differed greatly from the others The almost significant correlation was therefore of no explanatory value

In this material it could neither be demonstrated nor precluded that forced-out bone marrow was of importance for the increase in the ABd area in the other sectors

On comparison between animals treated by reaming and by brushing it was found that in the most reamed sectors 2 and 4 the reamed animals showed an almost significantly lower difference between the size of the CD areas on the treated and control sides than the "brushed animals In the other sectors no such difference was found

This indicates that the reaming in itself gives no essential increase of the intracortical avascularity compared with operations which give the same degree of trauma in the medullary cavity

tory value for the increase in the ABd area This could be due either to the fact that this increase was not influenced by changes in the size of the CDd and DEd areas, or to the fact that an existing relationship was obscured by other, more dominating factors It should also be emphasized that a true relationship might be difficult to demonstrate in view of the relatively small size of the material

On analysis of the correlation between the ABd values in individual sectors, it was found that the increase in the ABd values in certain sectors *differed considerably from that in the other sectors This was true in particular* for sector 2 (dorsal) in section 3, and to a smaller degree for sector 3 (fibular) and sector 4 (ventral) in section 2 It seems probable that the increase in the ABd values in these three sectors was highly influenced by other factors than those which produced an effect in the other sectors The difference was most clearly evident when the three sectors in question were compared with the sections in sector 1 which were highly correlated with one another The deviating reactionary pattern in these sections was found to be due to anatomical conditions On dissection of this area it was found that the dorsal sector of section 3 was taken from the area immediately distal and dorsal to the outer opening of the primary nutrient foramen in the bone, above the fibulo–tibial synostosis A fascia is attached ventral to the foramen and this should mean that marrow which was forced out through the foramen became localized dorsally on the tibia in the area from which the dorsal sector of section 3 was taken The fibular and ventral sectors of section 2 were taken from the area immediately distal and ventro distal to the outer openings of the secondary nutrient foramen and emissary foramen A fascia shields these openings here from the dorsal sector and this should mean that marrow forced out through these canals would have become localized fibularly and ventrally and may possibly have influenced the increase in the ABd values in these two sectors The high correlation between these two latter sectors supports the assumption that they were influenced by the same dominating factors The weak correlation between the dorsal sector in section 3 on the one hand and the fibular and ventral sectors in section 2 on the other supports the view that the ABd increase in these two groups of sectors was influenced by different dominating factors, *probably by bone marrow which was forced out through different* canals in the bone

The analysis of the correlation between the three ABd values discussed above and the remaining ABd values thus supports the assumption that the increase in these three ABd values was influenced by forced out bone marrow The results of the morphological studies reported in chapter 3 also support this view

In this material it could neither be demonstrated nor precluded that forced out bone marrow was of importance for the increase in the ABd area in the other sectors

On comparison between animals treated by reaming and by brushing it was found that in the most reamed sectors 2 and 4 the reamed animals showed an almost significantly lower difference between the size of the CD areas on the treated and control sides than the brushed animals In the other sectors no such difference was found

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CHAPTER 6

The Effect of Reaming and Brushing of the Medullary Cavity on the Diaphysis of the Dog Femur

In chapter 3 a study was described of the effect of reaming of the medullary cavity and of brushing out of the bone marrow in the tibial diaphysis in the rabbit In order to determine whether there were any differences in this respect between the rabbit and the dog corresponding investigations were also performed on the dog The femur was used for these experiments

Material

For the experiments 11 adult mongrel dogs were used (Table 15) The femur was chosen as the experimental bone since the tibia was used in these animals for studies of the healing pattern in compression osteosynthesis

Methods

The dogs were anaesthetized with Nembutal® (Abbott for veterinary use) given intravenously until the cough reflex was eliminated They were then intubated and ventilated with a mixture of oxygen and nitrous oxide

After shaving the skin and washing with spirit the trochanter major was exposed through a lateral incision The medullary cavity was opened with an awl medially to the trochanter major and was then widened 3–5 mm with hand driven reamers of the Kuntscher model (see Kuntscher 1962) The reaming was performed down to the distal metaphysis of the femur

In two dogs the contents of the medullary cavity were removed with a bottle brush about 2 cm thick which was moved up and down in the cavity three times

In order to label the newly formed bone Terramycin® (Pfizer) was injected intraperitoneally in a dose of 50 mg/kg body weight The time points of the injections in relation to the operation can be seen in Table 15

At the end of the experiment the animal was again anaesthetized and was given an intravenous injection of 500 U Heparin (Vitrum) per kg body weight A catheter with an inner diameter of 1 5 mm was inserted in the external carotid artery in the direction towards the heart. Through this catheter a suspension consisting of 200 ml Pelikan Indian ink in 800 ml isotonic NaCl was infused under pressure with an ordinary Record syringe After infusion of 100–200 ml the animal usually died The infusion was then continued for a further few hours at a slow rate until 5 litres of the Indian ink mixture had been given During the infusion the dog was kept in an

Table 15 *Dogs used for morphological studies The observation times and the times of labelling after the operation are presented*

L indicates the left femur R the right femur

Animal no	Observ time	Terramycin labelling on days after the operation		
		label 1	label 2	label 3
40	1 day			
44	2 days			
7L	7 days	5		
19	13 days	7	13	
14	14 days (2 weeks)	6	12	
7R	21 days (3 weeks)	7	19	
8	28 days (4 weeks)	7	26	
9	35 days (5 weeks)	7	33	
13	42 days (6 weeks)	9	39	
12	49 days (7 weeks)	10	47	
10	56 days (8 weeks)	7	21	40
11	70 days (10 weeks)	10	56	

upright position so that the grains of Indian ink would be deposited in as many blood vessel branches as possible in the freely dependent legs

After the Indian ink infusion the femur was exarticulated at the hip joint and freed from soft tissues After fixation for a few days in neutral 10% formalin the bone was frozen and in this state was divided the middle 5 cm being taken for examination From each end of this 5 cm a 1 cm thick slice was sawn off and used for the preparation of histological sections and angiographic sections according to the Spalteholz method A further 1 cm slice was then sawn off from each end of the specimen and these parts were embedded in methyl metacrylate and used for the preparation of fluorescence sections The remaining part of the middle specimen was used in some cases for the preparation of Sudan-stained frozen sections

The Spalteholz angiography sections were studied in a stereomicroscope and the fluorescence sections in an ordinary microscope under ultraviolet illumination as described in chapter 2

Results after Reaming of the Medullary Cavity

General Reaction

As a rule the animals began to stand carefully on the treated leg a few days after the operation and were able to bear full weight on the leg about 1 week postoperatively In no case was there any clinically manifest infection

Fluorescence Microscopic Studies

Observation time 7 days

Labelling on day 5 after the operation

Periosteum Around the diaphysis of the femur there was a narrow flu

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blood vessels with thick walls The bone trabeculae, as well as the endosteal surface of the cortex in the same area were doubly labelled with an inner yellow fluorescent and an outer red fluorescent band In this area the blood vessels and endosteal bone trabeculae had thus not been destroyed completely by the reaming In the medullary cavity central to this region newly formed bone trabeculae were seen Of these the trabeculae located nearest to the endosteum showed massive yellow fluorescence in the central regions and were covered with a red fluorescent band Further inside the medullary cavity were other bone trabeculae the central parts of which showed massive red fluorescence

Observation time 2 weeks

Labelling on days 6 and 12

Periosteum The periosteum was active and formed trabecular bone around almost the entire diaphysis The newly formed bone was up to 2 2 mm thick From labelling 1 a layer of newly formed bone with a maximal thickness of 400 μ was labelled In the peripheral parts of the trabecular bone the trabeculae were narrow and surrounded by an abundance of perivascular soft tissue In this area the trabeculae were homogeneously fluorescent from labelling 2 In the middle layer of the newly formed bone the trabeculae were wide the perivascular soft tissue sparse and the blood vessels narrow The central parts of the trabeculae were unlabelled while ring shaped labelling was seen around the vessels In the inner layer of the trabecular bone the trabeculae were homogeneously fluorescent from labelling 1 In this part there were numerous narrow long cavities the walls of which were partly unlabelled by labelling 2 and in the unlabelled parts the walls were often rough—a sign of bone resorption

Cortex In the cortex especially in its inner areas resorption cavities were observed the walls of which were partly covered by newly formed fluorescent bone and partly by narrow labelled areas indicating resorption The newly formed bone was often seen on the peripheral wall

Medullary cavity There was an abundance of newly formed trabecular bone in the medullary cavity Many of the bone trabeculae adjacent to the endosteum showed superficial resorption

Observation time 3 weeks

Labelling on days 7 and 19

Periosteum Superficial resorption was in progress around the entire diaphysis From labelling 1 a band of even thickness around more than half of the diaphysis as well as occasional beams between the blood vessels

orescent band of newly formed bone, of almost even thickness Outside this band, non-fluorescent bone and osteoid was seen The largest amount of unstained bone was found in the tibial part, where trabecular bone up to 250 μ high had been formed

Cortex In the middle part of the cortex numerous small resorption cavities which contained blood clots were seen In some of these cavities, there were narrow, Indian ink filled blood vessels All resorption cavities lacked fluorescence labelling of the walls

Medullary cavity Newly formed bone trabeculae the central parts of which were fluorescent were found in the dorsal part of the medullary cavity adjacent to the endosteum In other parts of the medullary cavity where newly formed blood vessels filled with Indian ink had invaded the medullary cavity from the cortex, bone fragments were found which had been released from the cortex by the reaming The surfaces of the bone fragments were rough and many showed a thin fluorescent layer on the surface

Observation time 13 days

Labelling on days 7 and 13

This dog died during the intravenous infusion of alizarin which in this experiment was used for labelling 2 Angiography was therefore not performed

Periosteum Active bone formation was observed around the entire diaphysis The new bone consisted mainly of trabecular bone, but primary osteones were also found in some areas From labelling 1 trabecular bone was labelled around a large part of the diaphysis but in some areas primary osteones or circumferential lamellae were labelled The peripheral parts of the trabecular bone showed diffuse alizarin labelling but in the inner parts there were ring shaped labelled areas around the blood vessels Adjacent to the surface of the original cortex several large cavities were found some of which continued into the original cortex

Cortex In several areas adjacent to the medullary cavity resorption cavities were found, the rough surfaces of which showed a thin zone of alizarin labelling which was considered to be a sign of resorption In other parts of the cortex osteones were found with an outer even fluorescent yellow Terramycin ring and an inner relatively thick even red ring of alizarin These formations were osteones which were becoming closed Some cavities showed yellow fluorescent bone deposits in one part of the wall and red resorption fluorescent layers in other parts

Medullary cavity In the dorsal area broad bone trabeculae were found, communicating with the original cortex and between these there were some

blood vessels with thick walls The bone trabeculae as well as the endosteal surface of the cortex in the same area were doubly labelled with an inner yellow fluorescent and an outer red fluorescent band In this area the blood vessels and endosteal bone trabeculae had thus not been destroyed com pletely by the reaming In the medullary cavity central to this region newly formed bone trabeculae were seen Of these the trabeculae located nearest to the endosteum showed massive yellow fluorescence in the central regions and were covered with a red fluorescent band Further inside the medullary cavity were other bone trabeculae the central parts of which showed mas sive red fluorescence

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had become labelled From labelling 2 ring shaped osteones which were becoming closed, were labelled The periosteal reaction appeared to have been strongest over the lateral part of the bone corresponding to the area where the bone had been affected most by the reamer from the inside

Cortex In the cortex there were rather few small resorption cavities some of which showed active bone formation on the wall Other cavities were unlabelled or exhibited a thin area of labelling indicating resorption Three fairly large pear shaped resorption cavities were observed which from the periosteal surface were eroded into the original cortex under the area where considerable periosteal bone formation had taken place previously No doubly labelled osteones were seen in the cortex

Medullary cavity In the dorsal part doubly labelled endosteal bone and some doubly labelled newly formed bone trabeculae were seen There was active bone formation on the bone trabeculae in towards the centre of the medullary cavity in several areas Close to the endosteum many parts of the bone trabeculae were undergoing resorption, at the same time as other parts of the trabeculae showed active bone formation

Observation time 4 weeks

Labelling on days 7 and 26

Periosteum Superficial resorption was taking place around the entire diaphysis The periosteal reaction appeared to be strongest fibularly and tibioventrally From labelling 1 the cross section showed fluorescent spicules between intermediate vessels and in some cases bridges over the vessels On labelling 2 most of the primary osteones which had formed after the operation had become closed but in some of them a small fluorescent ring had formed close to the blood vessels The bone which was fluorescent from labelling 1 also showed extensive superficial resorption In those areas where the callus was thickest, long narrow resorption cavities were found adjacent and parallel to the original cortex

Cortex Pronounced reconstruction was taking place in the entire cortex In longitudinal sections several cutter heads were observed A small number of doubly labelled osteones were seen in the outer and middle parts of the cortex In the inner part of the cortex mainly single labelled osteones were found

Medullary cavity In the central parts of the medullary cavity active trabecular bone formation was seen in towards a homogeneous almost structureless area which was invaded by narrow vessels In the peripheral parts of the medullary cavity there was extensive resorption of trabecular bone but bone formation on the trabeculae was also seen

Observation time 5 weeks

Labelling on days 7 and 33

Periosteum In the fibular part there was a prominence of newly formed bone The periosteum over its peak was inactive but slight periosteal new lamellar bone formation was seen on the one side of the prominence The prominence consisted of primary osteones in which some of the narrow blood vessel canals were surrounded by a narrow ring shaped fluorescent area while other osteones were completely closed at labelling 2

Cortex In the cortex numerous small cavities were seen which were completely or partly lined with newly formed fluorescent bone

Medullary cavity In the central part of the medullary cavity there was a structureless sparsely vascularized area This was partly surrounded by a thin border of trabecular bone the bone trabeculae of which were directed inwards towards the structureless area On the tips of the trabeculae which were directed in towards the centre an active deposition of bone was taking place while the peripheries of the trabeculae were undergoing resorption In the remaining parts of the medullary cavity there were only widespread fragments of bone trabeculae undergoing resorption on which sporadic bone formation was also observed

Observation time 6 weeks

Labelling on days 9 and 39

Periosteum Superficial resorption was taking place around the entire diaphysis The fluorescence labelling showed that after the reaming primary osteones had formed but these had been largely reabsorbed

Cortex Very active reconstruction was taking place in the cortex

Medullary cavity Th picture was similar to that from the animal observed at 5 weeks The resorption of the bone trabeculae in the centre of the medullary cavity was so active that even the bone which was labelled by labelling 2 given 3 days before the angiography was undergoing extensive resorption

Observation time 7 weeks

Labelling on days 10 and 47

Periosteum Superficial resorption was taking place around the whole diaphysis Fluorescent ring-shaped structures around the blood vessels were seen from labelling 1 At the time of labelling 2 the first formed primary osteones were completely closed

Cortex Very active reconstruction of the entire cortex was taking place but no doubly labelled osteones were observed in the inner part of the cortex

Medullary cavity The preparation had about the same appearance as that observed at 6 weeks

Observation time 10 weeks

Labelling on days 10 and 56

Periosteum Periosteal bone formation with the development of lamellar bone was seen in a few areas, but otherwise extensive superficial resorption was taking place From labelling 1 there was fluorescence of the centres of the bone trabeculae which were formed after the reaming At labelling 2 the newly formed osteones were closed

Cortex Pronounced reconstruction of the entire cortex was taking place

Medullary cavity As in the preparations observed at 4, 5, 6 and 7 weeks there was a structureless area in the medullary cavity, penetrated by occasional blood vessels The structureless area bordered onto normal fatty bone marrow or the endosteal surface of the original cortex

Microangiographic Studies

Observation time 1 day

Periosteum The blood vessels in the periosteum were well filled with Indian ink, rather tortuous and appeared wider than normally especially in the fibular part of the preparation

Cortex Approximately one third of the inner part of the cortex was avascular The vascular damage was greatest in the fibular part where most bone had been removed from the endosteal surface on reaming The blood vessels in the outer part of the cortex were usually well filled The same Haversian canal often contained two blood vessels, of which one, which was narrower and massively filled with Indian ink, was considered to be an arteriole while the other, which was wider and often only lined with Indian ink, was considered to be a venule

Medullary cavity The medullary cavity was filled with a blood clot Bone appeared to have been removed from the entire endosteal surface by the reaming In the ventral and dorsal parts there were blood vessels which penetrated the whole cortex up to but not into the medullary cavity In front of the mouth of the blood vessel there was a minor extravasation of Indian ink into the medullary cavity

Observation time 7 days

Periosteum In the tibial sector of the preparation an intensive periosteal vascular reaction was observed The blood vessels were mutually parallel and ran at right angles to the surface of the cortex They were convoluted

and showed calibre variations On several levels there were anastomoses between adjacent vessels In the remaining parts of the periosteum there were tortuous well filled blood vessels which ran mainly parallel with the bone surface

Cortex In the tibial sector of the bone about $^1/_{10}$ of the cortex was avascular In the remaining parts the cortex was vascularized and the intracortical blood vessels were usually well filled with Indian ink

Medullary cavity About one-quarter of the medullary cavity contained blood vessels Blood vessels grew from the cortex within the ventral and dorsal sectors in the areas where the endosteum did not appear to have been damaged by the reamer Several types of blood vessels were found in the medullary cavity Nearest to the endosteum a small number of anastomosing vessels of even calibre and up to 200 μ wide which were lined with grains of Indian ink were seen Central to these were blood vessels about 40 μ wide of even calibre and lined with Indian ink which anastomosed abundantly In the area bordering on the non revascularized part of the medullary cavity there were convoluted vessels about 5–40 μ wide and massively filled with Indian ink of similar appearance to those vessels observed in the rabbit at an early phase of revascularizaton of the medullary cavity and subperiosteal haematomas (see p 69)

Observation time 2 weeks

Periosteum There was a very strong vascular reaction around almost the entire diaphysis The blood vessels in the up to 2 mm thick vascular layer ran mainly perpendicular to the surface of the cortex and showed numerous mutual anastomoses In the outermost part of the vascular layer the blood vessels were convoluted and varied in calibre In the middle part of the layer the vessels were usually of equal calibre about 20 μ wide and straight Nearest to the original cortex in the areas where the thickest periosteal vascular reaction occurred there were blood vessels of equal calibre about 100 μ wide lined with Indian ink These vessels ran mainly parallel with the surface of the original cortex They were of the same type as were observed during resorption in periosteal and endosteal callus in the rabbit

Cortex About half of the cortical cross section area was avascular In some areas the entire cross section was avascular but in the dorsal sector the cortex was completely vascularized Some of the blood vessel canals in the vascularized part of the cortex were considerably wider than in the non vascularized part The canals often contained two blood vessels In longitudinal sections loops of blood vessels leading to "cutter heads and to broom shaped vascular proliferations were observed

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Observation time 7 days

Periosteum In the tibial sector of the preparation an intensive periosteal vascular reaction was observed The blood vessels were mutually parallel and ran at right angles to the surface of the cortex They were convoluted

Medullary cavity The medullary cavity was completely revascularized Adjacent to the endosteum the vascular structure was as in normal bone marrow and inside this the same types of ve sels as de cribed at an observation time of 4 weeks were seen

Observation time 6 weeks

Periosteum No periosteal vascular reaction was observed

Cortex Active reconstruction was taking place in the cortex which was almost completely vascularized

Medullary cavity The medullary cavity was revascularized The angiographic picture was similar to that at an ob ervation time of 5 week

Observation time 10 weeks

Periosteum No definite periosteal vascular reaction was ob erved

Cortex The entire cortex was vascularized Pronounced reconstruction of the whole cortex was taking place and several vessel loops in cutter heads were seen

Medullary cavity The medullary cavity was revascularized In the peripheral parts of the medullary cavity the vascular structure was normal More centrally there were fragments of bone trabeculae which lay in close contact with blood vessels up to 200 μ wide and lined with grains of Indian ink In the central part of the medullary cavity there was a structure less area criss-cros ed with vessels of the previou ly described type A normal vascular structure was seen in some areas in direct contact with the homogeneous central region

Studies of Histological Azan stained Sections

The histological studies were concentrated to the central area of the medullary cavity in animals with an observation time of more than 3 weeks On the fluorescence microscopic and angiographic preparations an almost homogeneous area containing a sparse number of relatively narrow blood vessels was seen at this location

Azan stained histological sections showed that the structureless area consisted of densely situated essentially parallel collagen fibre in which occasional cells cell aggregations and blood vessels were interspersed Between this connective tissue and the surrounding bone trabeculae there was a layer of cells with large nucl i Collagen fibres ran from the bone trabeculae into the fibrous tissue In other areas at an observation time of more than 5 weeks practically normal bone marrow or endosteal surface of the cortex bordered directly on to the fibrou ti sue without any intervening layer of cells (Color pl 2 b) At an ob ervation time of 10 weeks the active bone formation at the border to the fibrous scar tissue had stopped

cularized The same types of blood vessels were seen as in preparations observed at 1 week

Observation time 3 weeks

Periosteum The blood vessels in the periosteum were tortuous and dilated

Cortex About half of the fibular sector of the cortex was avascular In some preparations blood vessels had grown through the cortex into the medullary cavity even in areas where the reamer had removed bone from the endosteal surface

Medullary cavity The medullary cavity was almost completely revascularized Nearest to the endosteum there was a sparse number of the approximately 150 μ wide blood vessels which were described in preparations observed at 1 week In front of these, vessels of similar appearance but about 40μ wide were seen Central to these vessels on the border with non revascularized parts of the medullary cavity, anastomosing vessels were seen which were massively filled with Indian ink and which gave an impression of greater maturity than the blood vessels seen in corresponding areas in the animal observed at 1 week in that they were of more equal calibre and less tortuous

Observation time 4 weeks

Periosteum Dilated and tortuous periosteal vessels were observed in the fibular sector which was most affected by the reamer In other parts there was no definite increased vascular reaction

Cortex The cortex was almost completely vascularized In longitudinal sections vascular components of many cutter heads were observed

Medullary cavity The medullary cavity was completely revascularized In the peripheral parts there were large blood vessels up to 200 μ wide In the middle layer blood vessels about 40 μ wide were seen In the centre of the medullary cavity there was an almost structureless area which was sparsely invaded by fairly straight blood vessels about 20 μ wide and massively filled with Indian ink as well as sparsely anastomosing vessels about 30 μ wide and lined with Indian ink

Observation time 5 weeks

Periosteum In the lateral sector there was a moderate number of dilated periosteal vessels Otherwise no vascular reaction was observed

Cortex The cortex was almost completely vascularized The intracortical blood vessels appeared narrower and of more equal calibre than the vessels in preparations from animals at shorter observation times

Medullary cavity The medullary cavity was completely revascularized Adjacent to the endosteum the vascular structure was as in normal bone marrow and inside this the same types of ve sels as de cribed at an observa tion time of 4 weeks were seen

Observation time 6 weeks

Periosteum No periosteal vascular reaction was observed

Cortex Active reconstruction was taking place in the cortex which was almost completely vascularized

Medullary cavity The medullary cavity was revascularized The angiographic picture was similar to that at an ob ervation time of 5 week

Observation time 10 weeks

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Cortex The entire cortex was vascularized Pronounced reconstruction of the whole cortex was taking place and several vessel loops in cutter heads" were seen

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the contents of the medullary cavity were removed with a brush about 20 fat droplets were observed in every section Many of the canals in the cortex in this femur were completely obliterated by fat

Summary and Discussion

Periosteum After reaming of the medullary cavity the periosteal structures reacted in all animals The blood vessels increased in calibre became more tortuous and were filled massively with Indian ink on angiography Vessels which ran perpendicular to the surface of the cortex were seen at observation times of 1 and 2 weeks The vascular reaction began to decline at 4 weeks and appeared to be greatest and to persist longest in the area where the cortex had been most affected by the reaming from the inside

The periosteal bone formation was very active throughout In all animals primary osteones or trabecular bone were newly formed during the first few weeks postoperatively The most abundant new bone formation appeared to take place in those parts of the cortex where most bone had been removed from the endosteal surface by the reaming In these areas the vascular damage in the underlying cortex seemed to be greatest Subsequently there was very rapid resorption of most of the newly formed bone The bone resorption was most pronounced between 2 and 8 weeks postoperatively At an observation time of 10 weeks some tendency to formation of lamellar bone was noted The Terramycin labelling showed that about 1 week after the reaming mineralized bone beams were formed between the blood vessels and in some cases bridges over the vessels The so-formed primary osteones closed successively during the following 2–3 weeks

Cortex The extent of the intracortical vascular damage varied The greatest damage to the vascular system was observed after brushing out of the bone marrow when about two-thirds of the cortex was seen to lack Indian ink filled vessels at subsequent angiography In one animal about one third of the cortex became avascular after the reaming The reason for the avascularity is at least in part that the contents of the medullary cavity are squeezed or embolized into the Haversian canals and occlude them The cortex appeared to become revascularized fairly quickly however On preparations from animals studied 4 weeks or longer postoperatively the cortex was almost completely vascularized The revascularization took place with the aid of cutter heads but a broom like vascular reaction which gave larger resorption cavities in the cortex was also observed In some cases resorption cavities had formed also in the subperiosteal part of the original cortex This occurred where there was a very strong periosteal reaction It was probably due to the fact that the blood vessels in the outer part of the cortex had also been damaged The rebuilding of the cortex as reflected in the

Results after Brushing out of the Medullary Content

Microangiographic Studies

Observation time 1 day

Periosteum The periosteal blood vessels were somewhat narrower and less tortuous than the vessels in preparations from the left femur, which had been reamed

Cortex About $^1/_{10}$ of the inner part of the cortex was avascular Many Indian ink filled vessels, *especially in the dorsal and ventral parts*, penetrated the entire cortex to the medullary cavity A little extravasation of Indian ink was seen in the medullary cavity just in front of their opening

Medullary cavity The medullary cavity was filled with a blood clot and no Indian ink-filled vessels were observed

Observation time 2 days

Periosteum The periosteal vascular reaction was stronger than in preparations observed at 1 day *The blood vessels were tortuous and massively* filled with Indian ink

Cortex About two-thirds of the cortex was avascular In the dorsal sector blood vessels were seen to penetrate the entire cortex as far as the medullary cavity

Medullary cavity The medullary cavity was filled with a blood clot and no Indian ink-filled vessels were observed

Histological Results after Reaming and Brushing

Studies of Fat stained Histological Frozen Sections

Observation time 1 day

In every cross-sectional preparation from the right femur where the content of the medullary cavity was removed with a bottle brush there were about 10 fat droplets, which obliterated Haversian canals in the inner part of the cortex In preparations from the left femur, where the contents of the medullary cavity were removed by reaming approximately the same number of fat droplets were seen localized in the same way

Observation time 2 days

In preparations from the control femur which was not operated on occasional fat droplets were observed obliterating Haversian canals in the inner part of the cortex In five cross sectional preparations a total of only three fat droplets was seen In preparations from the other femur from which

massive than around the tibia but this should not have influenced the results essentially

The periosteal reaction appeared to be stronger in adult dogs than in adult rabbits In all dogs woven bone in primary osteones or trabecular bone formed subperiosteally which is rather uncommon in adult rabbits The resorption of the newly formed bone also appeared to take place considerably more intensively in the dog than in the rabbit

The intracortical vascular damage in the dog as also in the rabbit varied greatly It is reasonable to assume that the degree of intracortical vascular damage in the dog was dependent to a large extent on the pressure increase which occurred in the medullary cavity during the operation which was found to be the case in the rabbit (see chapter 2) Thus an experiment with brushing out of the medullary cavity in the dog when a thick bottle brush was used gave rise to considerable vascular damage in the cortex The reamers used in dogs and which were hand-driven were so formed that they probably gave only a relatively small pressure increase in the medullary cavity The reamers used in the rabbit experiments on the other hand resembled more the mechanically driven reamers of the Kuntscher or AO type which are used in the clinic (See Muller *et al* 1965) Revascularization of the cortex appeared to take place more rapidly in the dog than in the rabbit but this opinion is uncertain since the primary vascular damage varied greatly The rebuilding of the cortex with the formation of secondary osteones appeared to be more intensive in the dog than in the rabbit

Reaming of the medullary cavity did not always result in complete destruction of the blood vessels in the diaphyseal medullary cavity in the dog which always seemed to occur in the rabbit This is probably due to the fact that the dog has endosteal bone trabeculae which protect the vessels nearest to the endosteum especially in the dorsal part of the medullary cavity while in the rabbit the endosteal surface in the diaphysis is quite smooth The medullary cavity becomes revascularized very rapidly in the adult dog and bone formation starts earlier than in the adult rabbit The same types of blood vessel were observed in the medullary cavity in both animals during revascularization In the central parts of the medullary cavity in the dog a fibrous cicatricial tissue sparsely interspersed by blood vessels was often observed This tissue was also seen in the rabbit but was less prominent there

number of secondary osteones increased continuously throughout the experimental period up to 10 weeks after the operation Practically the entire cortex including the subperiosteal part, was reconstructed In primarily avascular areas of the cortex the new bone formation in resorption cavities appeared to commence about 10 days after the operation

Medullary cavity In one case undamaged vessels were seen in the dorsal part of the medullary cavity after the reaming This seems to be due to the fact that during the reaming the vessels were protected by endosteal bone trabeculae which were not removed by the reamer Revascularization of the medullary cavity began quickly, usually first from blood vessels in the dorsal part of the cavity The first vessels to invade the medullary cavity were abundantly anastomosing vessels of varying calibre and massively filled with Indian ink, of the type observed in the rabbit medullary cavity in the early revascularization phase Koekenberg (1963) classified this type of blood vessel as type *3* (see p *76*) These vessels later underwent a change to relatively narrow abundantly anastomosing vessels of more equal calibre *around which* trabecular bone was *formed Newly formed bone in* the medullary cavity became fluorescent from Terramycin which was given *5 days after the operation Resorption of the newly formed bone trabeculae* adjacent to the endosteum was observed 1 week postoperatively These trabeculae were then *surrounded* by vessels of large calibre which appeared to become transformed to normal sinusoids when the bone trabeculae had become resorbed After an observation time of 2 weeks the type of immature vessel which was first seen in the medullary cavity was no longer present there and instead more mature vessels were seen close to the central as yet not revascularized part of the medullary cavity After an observation time of 4 weeks an area of connective tissue interspersed by sparsely anastomosing narrow vessels of which many were massively filled with Indian ink was observed mainly localized to the central part of the medullary cavity On preparations studied after a long observation time this fibrotic area seemed to be inactive It bordered directly on the normal medullary tissue or to the endosteal surface of the original cortex Whether the fibrous area would remain as a scar or whether it would be rebuilt later cannot be decided The absence *of cells between the fibrous area and normal marrow* tissue or cortex supports the former alternative however

Comparison between the Reaction in the Rabbit and Dog on Reaming of the Medullary Cavity

In the rabbit the investigation was performed on the tibia and in the dog on the femur The musculature around the femur is considerably more

On suction reaming or brushing of the medullary cavity the medullary blood vessels in the diaphysis of the bone were destroyed This was especially effective in the rabbit Furthermore on reaming bone was removed from the endosteal surface of the diaphysis On destruction of the medullary vessels the cortex was deprived of that part of its circulation which came from the medullary cavity When this destruction resulted from reaming between 10 and 60% of the cortical cross sectional area became avascular An approximately equal degree of avascularity occurred in the distal and proximal parts of the diaphysis In a few isolated sectors in some animals however practically all intracortical vessels were filled with Indian ink Suction as a rule resulted in considerably less cortical avascularity than reaming or brushing The loss of the medullary circulation is thus not an essential cause of the cortical avascularity after operations in the medullary cavity and there are other more important factors which are discussed below

Friction heat produced by the reaming is of no or very little importance as a cortex-damaging factor under the given experimental conditions On the other hand the increase in pressure which can occur during operations in the medullary cavity can be of great importance Pressure increases far exceeding the systolic blood pressure are produced very easily and one result is that bone marrow is forced into the intracortical canals and obstructs the blood circulation there It is also conceivable that pressure increases may result in tearing of the intracortical vessels so that the circulation is directly occluded or with less damage in the occurrence of secondary thrombosis

A good correlation was found between extensive cortical avascularity a large number of intracortical marrow emboli and a high intramedullary pressure produced by incautious reaming or brushing in the medullary cavity On the other hand only very slight cortical avascularity and few intracortical emboli were found for example on careful reaming or suction in the medullary cavity

These results thus indicate that if the medullary circulation is occluded without the intracortical vessels being obstructed by marrow or being directly damaged the periosteal vessels can maintain the circulation in almost the whole of the intracortical vascular bed It is improbable however that at an early stage after the operation the intracortical circulation is sufficient to nourish all bone tissue especially not in the cortex nearest to the medullary cavity The incomplete filling of the functioning intracortical blood vessels at observation times of less than 24 hours support this assumption

My conclusions on the ability of the periosteal vessels to take over the intracortical nutrition when the medullary vessels have been destroyed thus

General Discussion and Summary

Danis (1947) stated that in his experience diaphyseal fractures stably fixed with compression plate osteosynthesis heal without roentgenologically visible periosteal callus Several authors have since found that the amount of periosteal callus is related to the degree of stability The AO group aim also with their stable osteosyntheses at obtaining callus-free bone healing

On healing of femoral fractures stably fixed by intramedullary nailing after reaming of the medullary cavity, a large amount of periosteal callus is often formed, however, even if judging by clinical and roentgenological signs, the osteosynthesis remains stable On intramedullary nailing there is therefore some additional factor which stimulates the periosteal new bone formation

In order to study this problem under reliably stable conditions different surgical procedures (brushing suction, reaming) were carried out in the medullary cavity of the tibia in growing and adult rabbits and of the femur in adult dogs without the leg being fractured

The traumatization of the bone and its circulation which was produced by the operation in the medullary cavity induced characteristic reactions in the periosteum and cortex and in the medullary cavity itself Bone was formed subperiosteally among other places and the bone which was newly formed after the operation was labelled with tetracyclin the ultraviolet fluorescence of which was studied microscopically in plastic-embedded ground sections The microcirculation in the cortex was studied by angiography at the end of the experimental period and preparations treated according to the Spalteholz technique were examined by stereomicroscopy The extent of the intracortical vascular damage and the amount of periosteal newly formed bone were quantitated in cross-sections The development of the periosteal bone formation activity was evaluated by recording whether the surfaces of the bone sections were fluorescent or not and by measuring the thickness of the bone and osteoid which were formed on the days preceding the angiographic examination The pressure conditions in the medullary cavity were recorded on reaming and brushing and the temperature increase on reaming Conventionally stained histological preparations and Sudan-stained frozen sections of bone were studied

The methods of recording and measurement were found on testing to have good reliability

ink were found during the formation of circumferential lamellae Several layers of similar vessels developed during the formation of primary osteones Relatively straight, frequently anastomosing vessels at right angles to the cortex and often of considerable length preceded the formation of trabecular bone The vascular reaction was observed in the periosteum as long as the new bone formation or bone destruction there was increased, but during the process of maturation of the bone the vessels became narrower and straighter

The periosteal newly formed bone could be either lamellar or woven bone Lamellar bone which was present in circumferential lamellae and in some primary osteones was not reconstructed during the course of maturation In woven bone which was found in certain primary osteones and especially abundantly in trabecular bone resorption cavities were sometimes observed These cavities gave the impression of migrating in a central direction towards the medullary cavity Subperiosteally formed woven bone was not observed during the normal periosteal growth in rabbits of the ages studied This could therefore be regarded as pathological bone formation which only occurred during the first 2–4 weeks after the operation In some cases after partial superficial resorption it was later covered by deposition of lamellar bone The perivascular spaces between the primary trabeculae of woven bone decreased by the formation of lamellar bone on the trabeculae In this way the primary osteones closed during the course of about 4 weeks

The periosteal bone formation activity was of varying intensity at different times after reaming of the medullary cavity In the rabbit the activity in the treated tibia which in growing animals was maximal a few days after the operation had decreased at an observation time of 2 weeks to almost the same level as was noted at 4 and 8 weeks Also on the control side the periosteal bone formation activity varied A few days postoperatively it was high it decreased to a minimum at 2 weeks and then again increased The reduction of the activity in the control tibia meant that the difference in the bone formation activity between the treated and control tibias was greatest at an observation time of 2 weeks despite the relatively low activity observed at that time point in the treated tibias Owing to a subsequent increase in the activity in the control tibia there was a partial equilibration with the treated tibia at an observation time of 4 weeks Extensive superficial resorption at 2 weeks most pronounced in the control tibia but also considerable on the treated side also indicated that the activation to periosteal bone formation which was induced by the operation in the medullary cavity had almost ceased 2 weeks postoperatively In adult rabbits in which there was no appreciable spontaneous periosteal bone formation the formation of bone on the treated side was activated more slowly than in the

differ somewhat from those of many previous investigators Macnab (1958) McAuley (1958) and Gustilo *et al* (1964) thus considered that the periosteal vessels were unable to supply any part of the cortex, and Trueta & Caladias (1964) claimed that only the outer third of the cortex could be supplied by periosteal vessels de Marneffe (1951, 1953) considered that in the proximal part of the tibial diaphysis in the rabbit the periosteal vessels could only supply the outer part of the cortex but in the distal part of the diaphysis the whole cortex Gothman (1961) and Rhinelander & Baragry (1962) found that during the first days up to one week after destruction of the medullary vessels the intracortical vessels were filled very incompletely from periosteal vessels (according to the latter authors due to the fact that normally many intracortical vessels are resting) but that the periosteal vessels were then able to take over the circulation in the cortex

The differences in the conclusions may be due to the fact that these investigators used Micropack as perfusion medium which seems to have difficulty in passing through the vessels in the subperiosteal bone before they have increased in calibre about one week after the operation They may also be due to the fact that a pressure increase was produced in the medullary cavity in their experiments resulting in marrow emboli in the intracortical vessels but that sufficient consideration was not taken of these factors

On increase in pressure in the medullary cavity bone marrow can be forced through canals in the cortex and deposited subperiosteally or transported further into the venous system to be filtered mainly in the lungs The transport of bone marrow through the cortex takes place most easily through the canals for the large vessels (canals for the primary and secondary nutrient arteries and the emissary vein) The marrow can often be observed macroscopically as a subperiosteal haematoma around the outer openings of these canals Embolism in the lungs can especially on brushing of the medullary cavity be so extensive that the animal dies during the operation

Operations in the medullary cavity induce characteristic reactions in the periosteum cortex and medullary cavity and these will be discussed separately

Periosteal Reaction

In the periosteum the blood vessels react earlier than the osteogenic cells (Wray, 1963, Trueta 1963) The morphology of the newly formed bone in the present study varied with the vascular reaction Convoluted vessels in one or a few layers, parallel with the cortex and massively filled with Indian

It has been considered that stimulating substances or the loss of inhibitory substances from the underlying cortex whose circulation has deteriorated may initiate periosteal bone formation Such a stimulating substance named by Lacroix (1951) osteogenin has been considered by several investigators to be capable of stimulating osteogenesis even from immature mesenchymal cells (Levander 1938 Annersten 1940 Goldhaber 1961 Urist 1965 Trueta 1963 Burwell 1964 Puranen 1966)

On statistical analysis of a material studied at an observation time of 1 week in which the medullary cavity of the right tibia was evacuated by suction and of the left tibia by brushing or reaming it was not found however that the extent of the intracortical vascular damage or the amount of bone removed on reaming had any explanatory value for the amount of new bone formed by the overlying periosteum This was in spite of the fact that the amount of subperiosteally formed bone was on the average greatest on the left tibia where the cortical vascular damage was also the most extensive Since the medullary cavity was evacuated from both the left and right tibia however the results indicate that other factors than loss of the medullary circulation—which was postulated by Richany *et al* in 1965—were of importance for the periosteal bone formation One significant factor was probably the bone marrow which was squeezed out subperiosteally

Cortical Reaction

The cortical necrosis could not be delimited by histological methods Nuclear pyknosis occurred even in viable bone and even when the number of empty osteocytic lacunae was found to have increased in the central and inner parts of the cortex with increasing observating times nuclear material was still observed in the inner avascular part of the cortex during an observation period of at least 4 weeks Neither could any well defined borderline be drawn between nucleated and non nucleated areas in the cortex The cortical damage caused by the reaming and other operations in the medullary cavity was therefore evaluated on the basis of the Indian ink filling of the intracortical vessels in preparations studied at short observation times

In that part of the cortex which had retained its circulation after the operation many of the blood vessels increased *in calibre* during the first week postoperatively and during the second week the bone canals around these vessels widened Many of the bone canals began to close again however after an observation time of about 4 weeks and in this way the circulation from the periosteum through the outer part of the cortex to its inner part and to the medullary cavity became concentrated to a number

growing animals and reached its maximum about 2 weeks after the operation

All rabbits, both growing and adult, formed more bone subperiosteally in the treated tibia than on the control side The amount of newly formed bone varied greatly between different animals In the growing animals bone was formed on the treated tibia mainly during the 2nd week postoperatively and on the control tibia during the 3rd and 4th weeks In the adult animals a considerably smaller amount of bone was formed than in the growing animals and an almost significant increase in bone formation on both tibias was only obtained when animals observed at 1–4 weeks were compared with those observed at 8 weeks

The cause of the increased periosteal bone formation could only be partially elucidated in this investigation and appeared to some extent to differ for the formation of lamellar bone and the formation of woven bone

The formation of lamellar bone which is the most usual type of periosteal bone formation in the rabbit after operations in the medullary cavity, appears to be an acceleration or revival of normal bone formation where the age of the animal and the degree of stimulation determine whether circumferential lamellae or primary osteones are formed Mature lamellar bone is homogeneous, is not rebuilt and appears also in other respects to be primarily adapted to mechanical demands on the skeleton It is not clear in what way this bone formation is stimulated but no findings have contradicted the view that it takes place by the mediation of growth and thyroid hormones (Frost 1963) or space polarizing factors (Frost 1963 Schenk 1965) Local stimulating factors cannot be excluded however

Woven bone especially when it was formed in a large quantity which occurred for example, in trabecular bone was found most commonly in those areas where as a result of the increased intramedullary pressure during the operation considerable amounts of bone marrow were sometimes forced out subperiosteally The formation of woven bone especially when it occurs in trabecular bone thus seems to be promoted by this subperiosteally forced out bone marrow Urist & McLean (1952) and Burwell (1967) showed, in transplantation experiments that cells in the bone marrow stimulated by necrosing cortical bone could be induced to form ossicles These ossicles have a great resemblance to the cavities in trabecular callus tissue which were observed in the present material Zucman *et al* (1968) found that bone marrow which had become localized subperiosteally was accompanied by considerable local bone formation Frost claimed (1963) that the formation of woven bone is governed by local factors and not by growth and thyroid hormones and that it has to be reconstructed in order to attain full resistance to mechanical stress

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of larger vessels, which thus took over the function of the destroyed nutrient artery Those parts of the cortex which had become avascular at the operation were revascularized by cutter heads' and broom shaped vascular proliferations The main revascularization did not appear to take place until after 2 weeks postoperatively Shortly afterwards bone formation began in resorption cavities often located in parts of the cortex rendered avascular by the operation After 8 weeks the cortex in growing animals was essentially revascularized while non revascularized areas were still found in the inner part of the cortex in adult animals at the longest observation time of 12 weeks In cases with very extensive intracortical vascular damage there was a tendency to sequestration of the innermost part of the cortex

Medullary Cavity Reaction

After brushing or suction the medullary cavity was filled with a clot which contained fragments of disintegrated bone marrow and, after reaming also bone fragments Occasional blood vessels were sometimes seen to penetrate the cortex from the periosteum, and appeared to be responsible for some local fluid circulation in the medullary cavity On revascularization of the medullary cavity the blood vessels usually grew out first from those areas of the cortex which had not been directly damaged by the reamer The first newly formed, immature vessels were observed in the medullary cavity about 1 week postoperatively The formation of bone trabeculae of woven bone began to take place close to more mature vessels about 30–40 μ in width which could be seen after an observation time of 3 weeks Resorption of the newly formed bone trabeculae, which began in the peripheral areas of the medullary cavity took place in the close vicinity of blood vessels about 100 μ in calibre which after the resorption of bone trabeculae appeared to be come transformed to normal sinusoids The same type of blood vessel was observed close to trabecular subperiosteally located bone, when callus cavities developed there A fibrous tissue which was localized as a rule with in the central areas of the medullary cavity and penetrated by narrow blood vessels, often developed in adult animals The cicatricial tissue did not appear to become completely rebuilt Foster (1951) observed such medullary fibrosis after a severe circulatory disturbance of the cortex and medullary cavity in adult rabbits while Branemark (1954) found that the bone marrow was completely restored in adult rabbits after scraping out of the contents of the medullary cavity

Comparison between Reaction in Rabbits and Dogs

A comparative investigation between the reaction on evacuation of the medullary cavity of the femur in adult dogs and the corresponding reaction

in the tibia of adult rabbits showed that the periosteum in the dogs reacted more intensively and that it always formed woven bone which was less common in adult rabbits After an observation time of 2 weeks there was very active resorption of the newly formed periosteal bone in the dog so that often only small fragments remained at an observation time of 4 weeks The intracortical vascular damage seemed to have the same origin in the dog as in the rabbit The reamers which were used in the main experiments viz hand driven reamers of the Kuntscher model (see Kuntscher 1962) probably gave rise to considerably smaller pressure variations in the medullary cavity however than those used in the rabbit experiments It is probably for this reason that the intracortical vascular damage seemed to be considerably le s extensive in the dogs than in the rabbits after reaming of the medullary cavity Brushing in the medullary cavity could result in avascularity of two thirds of the cortex however The reconstruction in the cortex was more active in the dog than in the rabbit The bone trabeculae in the medullary cavity in the dog appeared to be able to protect some of the endosteal blood vessels during the reaming Revascularization of the medullary cavity seemed to be initiated more quickly in the dog than in the rabbit but otherwise the courses were similar Fibrotic tissue which seemed to be at least partly permanent was found in the medullary cavity in all dogs at an observation time of more than 3 weeks

Complementary Investigations

A logical continuation of this work seemed to be to study how a cortical defect healed with intact and reamed medullary cavities I made such a study on the rabbit tibia It was found that when the medullary cavity was intact the defect was bridged over and filled in rapidly by woven endosteal bone Periosteal callus which also contained cartilage also quickly bridged over the defect and was concentrated to the area outside it When the medullary cavity had been destroyed the defect was first bridged over by periosteal callus which took place considerably later than when the medullary cavity was intact Callus was then often found around almost the entire bone but cartilage only outside the defect During the first 2 weeks of observation the amount of periosteal callus outside the defect was usually greatest when the medullary cavity was intact but at longer observation times it was greatest when the medullary cavity had been destroyed After destruction of the medullary cavity the defect was revascularized by blood vessels from the periosteum and outer soft tissues but was filled with callus considerably more slowly than when the medullary cavity was intact A detailed report of the results will be published in a separate paper

The increase in pressure in the medullary cavity and the subsequent intracortical and subperiosteal marrow emboli was found to be a very important factor for the occurrence of cortical vascular damage and periosteal new bone formation on operations in the medullary cavity A reduction of the pressure in the medullary cavity during the operation should reduce the marrow emboli and thereby decrease the intracortical vascular damage and the periosteal new bone formation Such an investigation, in which healing of an osteotomy in the rabbit tibia, fixed stably by compression nailing was studied, has been carried out (Olerud, Danckwardt-Lilliestrom, Lorenzi 1969) The pressure in the medullary cavity was reduced during the operation by suction through a drill-hole in the distal tibial metaphysis and the results were compared with a series without such a distal hole In the series with a peripheral drill hole to reduce the pressure there was less cortical vascular damage and less periosteal new bone formation than in the series in which the pressure was not reduced Primary bone healing over the fracture gap also occurred in the former cases

CHAPTER 8

Conclusions

From the series of experiments described in which the medullary cavity of the tibia in growing and adult rabbits and of the femur in adult dogs was destroyed by reaming brushing or suction the following conclusions could be drawn on the reaction of the diaphysis to these operations

1 The periosteal blood vessels were able to maintain circulation in practically the whole cortical vascular bed when the medullary vessels were destroyed

2 Pressure increase in the medullary cavity which was very easily produced at surgery to this cavity forced bone marrow into the intracortical canals and obliterated these to varying extents When large pressure increases occurred in the medullary cavity this took place within considerable areas of the cortex

3 The periosteal vessels reacted with increased filling with contrast medium and became tortuous Blood vessels which were mutually parallel and perpendicular to the surface of the cortex were present when trabecular bone was being formed

4 The periosteum reacted with increased bone formation In growing rabbits the periosteal bone formation activity increased to a maximum within a few days after the operation and the largest amount of new bone was formed subperiosteally during the second week postoperatively Adult animals reacted more slowly and showed maximal bone formation activity 2 weeks after the operation At an observation time of 2 weeks there was pronounced superficial resorption of the newly formed bone in growing rabbits

5 The periosteum formed either mature lamellar bone which was considered to be the result of an acceleration or revival of normal bone formation or woven bone which was believed to result from callus formation promoted at least partly by subperiosteally forced-out bone marrow The woven bone appeared to be a provisional callus in which reconstruction often began quickly and in which cavities with angiographically normal medullary sinusoids were formed These cavities seemed to migrate in a central direction with increasing observation times

6 The cortical necrosis could not be outlined by histological methods owing to the fact that nuclear material could remain in necrotic bone during an observation period of at least 4 weeks

The increase in pressure in the medullary cavity and the subsequent intracortical and subperiosteal marrow emboli was found to be a very important factor for the occurrence of cortical vascular damage and periosteal new bone formation on operations in the medullary cavity A reduction of the pressure in the medullary cavity during the operation should reduce the marrow emboli and thereby decrease the intracortical vascular damage and the periosteal new bone formation Such an investigation in which healing of an osteotomy in the rabbit tibia, fixed stably by compression nailing was studied, has been carried out (Olerud, Danckwardt-Lilliestrom, Lorenzi 1969) The pressure in the medullary cavity was reduced during the operation by suction through a drill hole in the distal tibial metaphysis and the results were compared with a series without such a distal hole In the series with a peripheral drill hole to reduce the pressure there was less cortical vascular damage and less periosteal new bone formation than in the series in which the pressure was not reduced Primary bone healing over the fracture gap also occurred in the former cases

CHAPTER 9

Statistical Methods

Notation

Number of cases $N=n$

$$\text{Mean } M=\bar{X}=\frac{\sum X_i}{n}$$

where X_i denotes the value for the *i*th case

Standard deviation

$$\text{S D}=\sqrt{\frac{\sum(X_i-\bar{X})^2}{n-1}}$$

Standard error of the mean

$$\text{S E}=\frac{\text{S D}}{\sqrt{n}}$$

Standard error of the difference between two means $\bar{X}$ and $\bar{Y}$

$$\text{S E}_{\bar{X}\bar{Y}}=\sqrt{\text{S E}_{\bar{X}}^2+\text{S E}_{\bar{Y}}^2}$$

Correlation analysis The correlation coefficient, r of x and y is defined by the expression

$$r=\frac{\sum(x_i-\bar{x})(y_i-\bar{y})}{\sqrt{\sum(x_i-\bar{x})^2\sum(y_i-\bar{y})}}$$

where $\bar{x}$ and $\bar{y}$ denote the means for the x and y series respectively

Significance tests

1 In testing whether a mean value differs from 0 the following approximately t-distributed ratio has been formed

$$t=\frac{\bar{x}}{\text{S E}_{\bar{x}}}$$

2 In testing whether the regression coefficients differed from 0 the method described by Cramer (1945) and Hald (1948) was used

A t value was produced from the expression $\frac{b_j}{\text{S E } b_j}$

7 The extent of the intracortical vascular damage and the amount of bone removed on reaming were not found to have any explanatory value for the amount of newly formed bone in the overlying subperiosteal are

8 Those parts of the cortex which had been rendered avascular by the operation were revascularized from the outer vessel containing parts of the cortex by means of cutter heads ' and broom shaped vascular prolifera tions and thereby underwent extensive reconstruction The areas of the cortex with residual circulation were *partly rebuilt the bone canals around* many of the blood vessels first becoming wider and then again decreasing in width when the circulation to the inner part of the cortex and to the medullary cavity became concentrated to a smaller number of vessels The cortex adjacent to the medullary cavity was revascularized also from vessels which had newly formed in the medullary cavity

9 The medullary cavity was revascularized mainly from vessels which in *the diaphysis penetrated the cortex from the periosteum In the medullary* cavity trabecular bone was formed close to 30–40 μ wide thin walled ves sels and was subsequently quickly resorbed in the close vicinity of vessels approximately 100 μ wide which were later transformed into angiographi cally normal sinusoids Small areas of dense fibrous tissue appeared to re main permanently in the medullary cavity

10 On comparison between the reaction of the diaphysis to destruction *of the medullary cavity in adult rabbits and adult dogs*, it was found that the periosteum reacted more intensively in the dog and always formed woven bone within some area which was relatively unusual in the adult rabbit The newly formed subperiosteal bone was resorbed very rapidly in the dog The cortical vascular damage appeared to have the same origin as in the rabbit but the cortical reconstruction was more extensive In the medullary cavity the same rebuilding process was seen as in the rabbit

CHAPTER 9

Statistical Methods

otation

Number of cases $N=n$

$$\text{Mean } M=\bar{X}=\frac{\sum X}{n}$$

here X_i denotes the value for the ith case

Standard deviation

$$\text{SD}=\sqrt{\frac{\sum(X_i-\bar{X})}{n-1}}$$

Standard error of the mean

$$\text{SE}=\frac{\text{SD}}{\sqrt{n}}$$

Standard error of the difference between two means $\bar{X}$ and $\bar{Y}$

$$\text{SE}_{X\ Y}=\sqrt{\text{SE}_X^2+\text{SE}_Y^2}$$

Correlation analysis The correlation coefficient r of x and y is defined by the expression

$$r=\frac{\sum(x_i-\bar{x})(y_i-\bar{y})}{\sqrt{\sum(x_i-\bar{x})^2\sum(y_i-\bar{y})^2}}$$

where $\bar{x}$ and $\bar{y}$ denote the means for the x and y series respectively

Significance tests

1 In testing whether a mean value differs from 0 the following approximately t distributed ratio has been formed

$$t=\frac{x}{\text{SE}}$$

2 In testing whether the regression coefficients differed from 0 the method described by Cramer (1945) and Hald (1948) was used

A t value was produced from the expression $\frac{b_j}{\text{SE } b_j}$

3 In testing whether a correlation coefficient differed from 0 the following ratio was produced

$$\frac{r}{\sqrt{1-r}}\sqrt{n-2}$$

which— if the true correlation was zero—was considered to be distributed like Student s t, with n-2 degrees of freedom

4 In testing differences between means, the following approximately t distributed ratio was formed

$$t=\frac{\bar{x}-\bar{y}}{\text{S E}_{\bar{X}-\bar{Y}}}$$

Significance levels

The term significant is used in accordance with the following convention If an observed difference between two means is of such magnitude that the probability, P, of obtaining a difference at least as great as the observed value is greater than 0 05 (where the null hypothesis is assumed to hold), then that observed difference is said to be non significant

If $0\ 01<P<0\ 05$ the difference is said to be almost significant and is marked*

If $0\ 001<P<0\ 01$, the difference is said to be significant and is marked **

If P $<0\ 001$ the difference is said to be highly significant and is marked***

Multiple regression analysis used in the present study

For a series of n experimental animals we wish to study the relation between a dependent variable y, called the regressand and constituting different *ABd* areas and a set of explanatory variables $x^{(1)}$ $x^{(2)}$ and $x^{(3)}$ The explanatory variables were similary localized *CDd* and *DEd* areas and also the type of operation

In order to study the relation between the y and x variables a type of equation must first be laid down Individual numerical values must also be available for each variable In the present work equations of the following form have been studied

$$y=b_0+b_1x^{(1)}+b\ x^{( )}+b_3x^{(3)}$$

where b_0 b_1 b b_3 are the coefficients which are to estimated In estimating these coefficients the principle of least squares has been applied

The principle of least squares has been described in detail by Cramer (1945) and Hald (1948) who also explain the method of calculating S E for the coefficients

Predicted value

The y value for an individual (i) predicted with the aid of the regression equation is defined as

$$b_0+b_1x_i^{(1)}+b_2x_i^{(2)}+b_3x_i^{(3)}$$

R = Correlation between observed y value and predicted y value

The regression analysis program

In treating the data as stated above the following regression analysis program was used Hodson Thornber Manual for (B34T 8Mar 66) a stepwise regression program Report 6603 Univ of Chicago March 1966 (stencil)

All statistical analyses were performed in collaboration with Associate Professor G Eklund Ph D at the Department of Statistics University of Stockholm

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a

b

Fig. 3 Distal fluorescence cross section observation time ? weeks. Growing animal. Labelled on day 0 and 1 postoperatively

(a) Control side. Subperiosteally circumferential lamellae are formed around two-thirds of the section. Reconstruction is taking place in the cortex, mainly new formation of bone

(b) Reamed side. Subperiosteally circumferential lamellae, primary osteones or ... bone are formed around almost the entire section. More bone has been formed subperiosteally than on the control side. Several areas in the central and middle parts of the cortex lack signs of new bone formation where such signs are present on the control side. This is a sign of *avascularity* there. In the ventro tibial ... of the section (above right) there are larger resorption cavities than on the ... side, partly with bone formation taking place on the walls

Plate ? (*a*) Di tal Spalteholz cross section observation time 2 weeks Growing animal
45 There i a strong periosteal vascular reaction with the formation of vessels
perpendi ular to the original cortex (formation of trabecular bone) except in the
central part of the entral sector (above) where several layers of convoluted vessels
have formed (formation of primary osteones) *Under the* palisade formed blood vessels
a *large* part of the original cortex is avascular and in several areas is undergoing
resorption from the surface of broom shaped vascular proliferations Under the con
oluted essel ventrally only the central part of the cortex is avascular Revasculariza
tion is taking pl ce here largely by cutter heads

(*b*) Azan stained histological section from a dog 5 weeks after reaming of the
medullary c vity In the middle of the section red stained trabecular bone is formed
close to the blue stained fibrous area. In other parts of the section the fibrous area
borders on old corti al bone or newly formed almost normal marrow This may in
dicate that the fibrous tissue will remain in its present state



Plate 2 (*a*) Di tal Spalteholz cross section, observation time 2 weeks Growing animal 45 There is a strong periosteal vascular reaction with the formation of vessels perpendicular to the original cortex (formation of trabecular bone) except in the central part of the ventral sector (above) where several layers of convoluted vessels have formed (formation of primary osteones) Under the palisade formed blood vessels a large part of the original cortex is avascular and in several areas is undergoing resorption from the surface of broom shaped va cular proliferations Under the con voluted essels ventrally only the central part of the cortex is avascular Revasculariza tion is taking place here largely by cutter heads"

(*b*) Azan stained histological section from a dog 5 weeks after reaming of the medullary cavity In the middle of the section red stained trabecular bone i formed close to the blue stained fibrous area In other parts of the section the fibrous area borders on old cortical bone or newly formed almost normal marrow This may in dicate that the fibrous tissue will remain in its present state

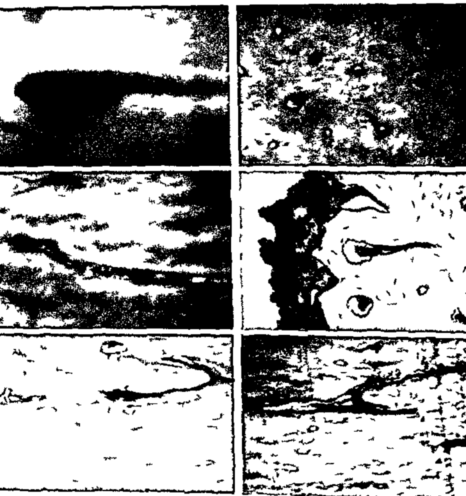


Plate 3 (*a*) Longitudinal fluorescence section of the diaphysis from an untreated tibia Animal 174 Labelled 2 days before angiography A cutter head with a vessel loop forming a secondary osteone

(*b*) Sudan stained cross section of rabbit tibia 1 day after brushing of the medullary cavity Several of the intracortical canals are filled with red fat stained material Other canals are empty or contain Indian ink filled vessels

(*c*) Sudan stained longitudinal section of rabbit tibia 1 week after reaming of the medullary cavity An intracortical canal is partly filled with Sudan stained material

(*d*) Sudan stained cross section of rabbit tibia 1 day after brushing of the medullary cavity Much Sudan stained material is located below the periosteum and in some intracortical canals

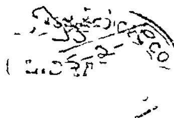
(*e*) Sudan stained longitudinal section of rabbit tibia 4 weeks after reaming of the medullary cavity A cutter head is revascularizing an osteone whose canal in front of the cutter head is obliterated by fat

(*f*) Sudan stained longitudinal section of rabbit tibia 4 weeks after reaming of the medullary cavity The intracortical canals have become widened Indian ink filled vessels have passed by the fat droplets which have not yet been resorbed

AUGUSTUS A. WHITE III

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AN EXPERIMENTAL STUDY OF AUTOPSY SPECIMENS

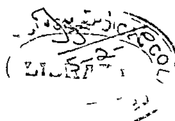


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Department of Orthopaedic Surgery
University of Gothenburg, Sweden

ANALYSIS OF THE MECHANICS OF THE THORACIC SPINE IN MAN

AN EXPERIMENTAL STUDY OF AUTOPSY SPECIMENS

By

AUGUSTUS A. WHITE III

MUNKSGAARD
Copenhagen 1969

To My Mother, My Late Father
and All Afro-Americans

GÖTEBORG 1969
ELANDERS BOKTRYCKERI AKTIEBOLAG

To My Mother, My Late Father
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CONTENTS

FOREWORD

The background events that ultimately lead to the production of this work take their origin several years ago at Yale Medical Center where the author was a resident in orthopaedic surgery. Interest in biomechanics was expressed at that time to his chief and friend Professor *Wayne Southwick*. As a result of the endeavours and encouragement of Dr Southwick arrangements were made for a fellowship to pursue this interest. Because of the outstanding work and reputation of Professor *Carl Hirsch* in the field of biomechanics he was approached regarding a position in his Department. Professor Hirsch has contributed generously to this project through his perspective, experience and stimulating discussions. This participation has been very much appreciated.

Acknowledgement is to be given for the valuable assistance of Docent *Svante Polander* and Doctor *Erland Lysell*, both of whom discussed constructively principles and techniques related to the project. Mr *Manohar Panjabi* has been a valuable and very essential consultant regarding engineering considerations and applied mathematics. The writer is grateful for the able participation of Mr *Lennart Beckmann* and Mr *Bengt Carlsson* in computer programming and Mr *Bo Ericksson* in statistical analysis. Ing. *Hans Hellstrom* has assisted tremendously in innumerable aspects of the project, as has Miss *Lena Johnsson* and Mrs *Inga Lisa Elver*. Their help is certainly appreciated. The author wishes also to express his gratitude to Professor *Jan Mellgren*, Docent *Bertil Stener*, Docent *Leif Lehman*, Docent *Alf Nachemson* and Assistant Professor *Mart Magi*. Miss *Margareta Apelskog* is to be thanked for secretarial work and Miss *Anita Nordqvist* for photographic assistance.

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Gothenburg, September 1969

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INTRODUCTION



It is as if one undertook for example to investigate a railroad accident solely from a study of the wrecked cars Much could be learned as to the effect and direction of th destructive forces the amount of force expended and the kind of damage done but more could be learned and future accidents could be better prevented by a study of the normal running time of the trains their proper relation to each other at the time of the accident and by an investigation of the signal system and the routine precautions adopted

This quote from Lovett s classic work on *The mechanisms of the normal spine and its relation to scoliosis* puts into perspective one of the most obvious clinical values of a study of the mechanics of the thoracic spine It applies with equal relevance to the practical problem of the effects of trauma on the thoracic spine Pain syndromes related to the thoracic spine though not as frequent as in the cervical and lumbar spine do present a significant clinical problem (*Hult* 1954 *Horal* 1969) Accurate reliable information about the normal is generally the basis if not the prerequisite for progress in the under standing and treatment of the abnormal

In the mechanical modelling of the human system one must have access to the relevant biomechanical data before the modelling process can be meaningful. Frequently however such data is simply not available or at least not in a form for direct use by the engineer or physical scientist interested in developing a mathematical model. With regard to the spine more attention appears to have been given to the behavior of the cervical and lumbar regions than to the thoracic region although as mentioned previously vertebrae in the thoracic region fracture more frequently than other vertebrae.

This above quotation from a dissertation by Orne and Liu in 1969 on *A mathematical model of spinal response to impact* points up quite nicely the more contemporary significance of a study of the machanics of the thoracic spine.

The goals of this investigation are to provide information about the mechanics of the thoracic spine in man. A review of the literature will show that previous studies on the thoracic spine have defined the relevant problems and provided the background for current investigations. However there are no studies which employ *precise modern* techniques, use *substantial* numbers of subjects and analyse *all* aspects of the movement of this important part of the vertebral column. It will be noted that there is considerable variance in the writings of previous authors as regards their description of some of the very basic factors involving the patterns and extent of movement in the thoracic spine. There are two precise and accurate methods which have been employed for analysis of motion of the spine. One has been used by *Rolander* (1966) on the lumbar spine. The other has been employed by *Lysell* (1969) on the cervical spine. As there are some differences in the information that can be derived from these two techniques both methods are employed in this investigation. Basic concepts of engineering mechanics play a significant role in the presentation and interpretation of this material. This will most probably be the case for subsequent works. Consequently an attempt is made to deal with the material in a manner meaningful to mechanical as well as biological interpretation.

There are several important questions the answers to which constitute a thorough descriptive analysis of the motion of the thoracic spine. These questions are:

1. What is the amount and the pattern of flexion and extension? What is the relative amount of each?
2. What is the amount and the pattern of lateral bending and rotation?
3. What are the cephalocaudal variations in the above mentioned patterns and quantities?
4. Is there coupling of axial rotation with lateral bending? What is the direction of the axial rotation?
5. Where are the "Centers of Motion" for the various movements?

6 Are there differences in the motion of the vertebrae when their posterior elements are removed?

The aim of the study is to provide through two separate experimental investigations information that will answer the preceding questions The first part is a two dimensional analysis in which the motion of one vertebra in relation to the fixed subjacent one is observed under controlled loads The second part is a truly three dimensional analysis of larger segments of the thoracic spine taken through their various ranges of motion

ANATOMIC CONSIDERATIONS RELATED TO MECHANICS

To follow is a recapitulation of those aspects of the anatomy that appear to be pertinent to the mechanical behaviour of the spine. A more extensive review of the anatomy is possible by referring to *Fick* (1904), *Strasser* (1913), *Braus* (1921), *Frazer* (1940), *Hollingshead* (1965) and *Gray* (1967).

Normal Curves and Regional Variations

In the frontal plane the spine appears straight and symmetrical with the exception of a very slight right convex thoracic curve. This is said to be due to the position of the aorta (*Steindler* 1955). Other writers suggest that it is due to increased use of the right hand (*Davis* 1918, *Frazer* 1940). The relation of handedness has been supported by the observation of left convex curvature in left handed individuals (*Gray* 1936). There are four normal curves in the sagittal plane. The mechanical value of the curves are increased flexibility with stability and augmented shock absorbing capacity. These curves are convex forward in the cervical and lumbar regions and concave forward in the thoracic and sacral regions (Fig. 2). The lumbar curve, quite aesthetically, is slightly more accentuated in the female. The thoracic curve is primary and can be looked upon as the persisting curve of the embryonic axis (*Frazer* 1940). The dorsal curve of the thoracic portion of the spine is due to the lesser vertical height of the anterior as opposed to the posterior border of the vertebral bodies (*Gray* 1967). This is also true for the sacral curve (Fig. 2). The thoracic curvature has been observed to increase with age. Below the age of 40 the female thoracic spine is straighter than that of the male. This difference is not found after 40 when the female's dorsal spine becomes as bent as the male's. Such change may contribute to the so called "dowager's hump" (*Loebl* 1967). The convexity of the cervical and lumbar regions is largely contributed to by the relative ventral thickness of the discs. Therefore, when distracting forces are applied to the entire spine there is a flattening of the cervical and lumbar lordosis. This is probably due to the deformation of the discs. At the same time the thoracic kyphosis, based on osseous asymmetry, is almost unaltered (*Kleusen* 1965).

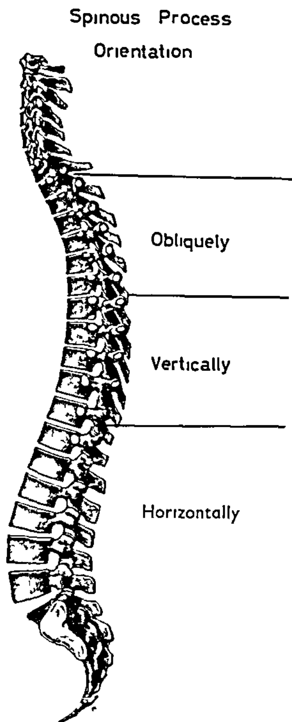


Fig 2 This demonstrates the normal curves of the vertebral column in the sagittal plane The orientation of the spinous processes is also pointed out (The drawing is reproduced from Gray's Anatomy 34th Edition London 1967 with permission of the publisher)

From the first cervical to the last lumbar vertebra the bodies increase constantly in mass (*Steindler* 1955 *Gray* 1967) In the frontal plane the width of the bodies of the vertebra increases from the second cervical to the third lumbar (*Gray* 1967) In the thoracic spine the sagittal and frontal diameters are about equal (*Gray* 1967) or slightly greater in the sagittal plane (*Strasser* 1913) Measurements by *Frazer* (1940) of outlines of upper surfaces of thoracic vertebrae revealed consistently greater frontal diameters In the upper three vertebrae this pattern of a greater frontal than sagittal diameter was more marked than in the lower vertebrae

Articular Facets and Spinous Processes

Winslow (1732) published probably the earliest definite contribution to the subject of motion in the vertebral column He included a meticulous description of the apophyseal facets and a discussion of their contact during movements of the spine *Humphry* (1858) pointed out that movements permitted in the spine are mainly due to the shape and position of the articulating processes of the diarthodial joints It is the orientation of these joints in space that determine their mechanical importance In the thoracic spine the superior facet is almost flat and directed backwards a little laterally and upwards The inferior facet is directed forwards slightly downwards and medially (*Gray* 1967) (See Figs 2 and 3) This orientation more or less aligns the plane of the joints along the arch of a circle lying in the transverse plane the center of which is in the vertebral body (*Pocknell* 1938) *Strasser* (1913) emphasized the variation of the slopes of the facets in different regions of the spine *Davis* (1959) studied nineteen vertebral columns two of which were freshly macerated from young adult males Using instruments with line markers at right angles to an edge which could be fitted over the facet he determined the

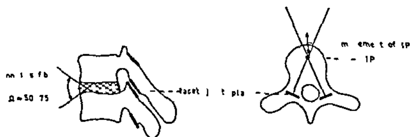


Fig 3 The diagram demonstrates the orientation of the articular facets in the horizontal and sagittal planes The intersection point (IP) of Davis and the geometrical arrangement of the annulus fibers are also shown

intersection points (IP) of lines perpendicular to the plane of the facets (Fig 3) In the upper two thoracic vertebrae this *point was found to* be well in front of the vertebral body As observations are made more caudally the point is found to approach and then enter the line of the vertebral bodies Even lower in the thoracic region the point again leaves but may re enter at the lowest thoracic joint The freedom of rotation in the thoracic region is thought to be related to this particular orientation of the facets in space (*Rockwell*, 1938, *Steindler*, 1955 *Lucas* and *Bressler* 1961) One witnesses an abrupt change in the orientation of the plane of the articular joints, when a comparison is made between the thoracic and the lumbar spine This occurs most commonly at the inferior facet of Th 11 or Th 12 but can be as high as Th 10 (*Gray*, 1967) Such a vertebra with the plane of the facet joint lying more sagittally than frontally will behave in motion like a lumbar vertebra

The spinous processes in the upper thoracic region are directed obliquely downwards in the middle they are longer and almost vertical In the lower thoracic and lumbar regions they are horizontal (Fig 2) In the thoraco lumbar region dorsiflexion is limited by the spinous processes (*Akerblom* 1948)

Intervertebral Discs

A number of writers have discussed the significance of the intervertebral disc in relation to the amount of movement between vertebrae (*Keller* 1924 *Beadle*, 1931 *Wiles*, 1935 *Steindler* 1955 *Lucas* and *Bressler*, 1961) This organ constitutes 1/3 of the length of the column (*Klausen*, 1965) *Gray* (1967) places this estimate at 1/5 The intervertebral disc is comprised of three parts the nucleus pulposus the annulus fibrosus and the cartilagenous end plate The gelatinous nucleus pulposus contrary to popular opinion is *not a noto cordal remnant* It is described as an area of *degenerated notocord invaded by fibrocartilagenous cells derived from intervertebral mesynchymal cells* (*Keyes* and *Compere* 1932 *Hollingshead* 1965) Microscopically it is composed of a very loose and translucent network of fine fibrous strands In this there are found a variety of connective tissue cells some spindle shaped others with clear vacuolar nuclei The latter *have been* thought to be decendants of the special cells of the embryonic chorda tissue (*Beadle* 1931) These connective tissue elements lie in a mucoprotein gel which contains various mucopolysaccharides (*Hirsch* *Paulson*, *Sylven* and *Snellman* 1953 *Happey* *McRae* and *Naylor* 1953 *Naylor et al*, 1955 *Naylor* 1962) The nuclear water content ranges from approximately 70–90% It is highest at birth and tends to decrease with age (*Naylor et al* 1955) The lumbar nucleus fills 30–50% of the total disc area in cross section (*Perey* 1957 *Nachemson*, 1960 *Eie* 1966) In the low back the nucleus is usually more posterior than central and lies about at the juncture of

the middle and posterior thirds of the sagittal diameter In general it is placed further forward in the thoracic region (*Beadle* 1931 *Joplin* 1935) The size of the nucleus as well as its capacity to swell is larger in the cervical and lumbar region and probably related to the greater flexibility there (*Beadle* 1931 *Gray* 1967)

The annulus fibrosus is a portion of the intervertebral disc which gradually differenciates itself from the periphery of the nucleus This structure is composed of fibrous tissue in concentric laminated bands approximately six in the thoracic spine (*Joplin* 1935) The collagen bands run obliquely from one vertebra to the next in a helicodial arrangement with the fibers in contigous laminae lying at angles of about 50–75 to each other (*Horton* 1958 *Naylor* 1962 *Galante* 1967) (Fig 3) The annulus fibers are attached to the cartilagenous end plates in the inner zone while in the more peripheral zone they attach like Sharpeys fibers directly into the osseous tissue of the vertebral body (*Hirsch* and *Schajowic* 1952) The third and final portion of the intervertebral disc is that of the cartilagenous end plate Comparatively little is known about this structure It is composed of hyaline cartilage and separates the other two components of the disc from the vertebral body (*Beadle* 1931 *Hirsch* and *Schajowic* 1952)

The above considerations complete the anatomic description of the disc and bring into focus some relevant mechanical properties of the organ The angular arrangement of the annulus fibers and their strong attachment to the vertebral end plates create mechanical conditions for strong resistance to horizontal translation (*Hirsch* and *Sonnerup* 1968) The disc in various mannerisms behaves with visco elastic properties (*Virgin* 1951) Loads lasting seconds give perfect elasticity curves of the same shape as those observed for hyaline cartilage If a disc is kept loaded a certain amount of compression occurs until equilibrium is reached (*Hirsch* and *Nachemson* 1953) When stress is applied to a normal or slightly degenerated disc the pressure per unit area is about 50% higher in the nucleus This is probably due to the elastic resistance of the fibers of the annulus The nucleus can be considered to be subject to Pascal s laws of fluids and consequently is hypothetically incompressible (*Keyes* and *Compere* 1932 *Joplin* 1935 *Inman* and *Saunders* 1947 *Nachemson* and *Elfstrom* 1969) Forces applied to the lumbar nucleus have been explained They are thought to be transmitted throughout the nuclear material with the forces exerted on the cartilagenous plate and the annulus being equalized The complete unit of nucleus and annulus is consequently somewhat analogous to a rubber tire with relatively high internal pressure (*Nachemson* and *Elfstrom* 1969) Compression of the disc thus results in a bulging of the annulus as observed by *Hirsch* (1951) and re evaluated and interpreted by *Polander* (1966) in the lumbar region of the spine *Horton* (1958) maintained that this increase in the

radius of the disc with compression is achieved by the movement of adjacent uniaxial sheets with consequent decrease in Ω (Fig 3) Loss of the elasticity of the disc is described by *Beadle* (1931) as the most conspicious change differentiating the old or middle aged spine from the young *Naylor et al*, (1955) observed in the aged annulus a loss of gel properties of the nucleus along with increased crystalization of its collagen fibers In the annulus crystalization changes as well as alterations in fibrillar orientation affected its biaxial structure This complex of changes in the disc associated with ageing was interpreted as affecting particularly the function of mobility, which is thought to be decreased in the aged

Ligaments

The major ligaments of the spine from anterior to posterior are as follows the anterior longitudinal ligament the posterior longitudinal ligament the ligamentum flavum (yellow ligament interarcuate ligament) the capsular ligaments the intertransverse ligaments the interspinous ligament and the supraspinous ligament The radiate ligaments anterior costotransverse intertransverse costae tubercle and posterior costotransverse ligaments are listed

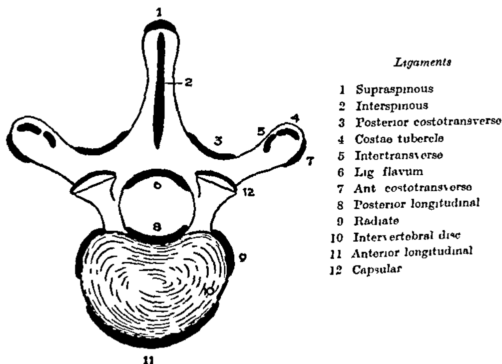


Fig 4 Diagrammatic review of ligaments in thoracic spine (From *Lucas* and *Bressler* 1961)

for the sake of completeness but will not be discussed further (Fig 4) The anterior longitudinal ligament arises from the tubercle of the occiput and is attached to the atlas and the anterior surface of all vertebrae down to and including a part of the sacrum It attaches firmly to the edges of the vertebral bodies but is not so firmly interwoven with the annulus fibers of the intervertebral disc (*Schmorl* and *Junghanns* 1932) The width of the anterior longitudinal ligament is diminished at the level of the disc It is more narrow and more thick in the thoracic region (*Gray* 1967) The posterior longitudinal ligament arises from the basilary portion of the occiput and runs over the posterior aspect of all the vertebrae down to the coccyx It too is interwoven with the intervertebral disc and thicker in the thoracic region It is however the converse of the anterior longitudinal ligament in that it is wider at the disc and narrower at the vertebral body *Tkaczuk* (1968) found both the anterior and the posterior longitudinal ligaments to be prestressed in the lumbar region

The ligamenta flava extend from the anterior inferior border of the lamina above to the posterior superior border of the lamina below (*Gray* 1967) They connect the borders of adjacent lamina from the second cervical vertebra to the first sacral vertebra (*Morris* 1879) The yellow ligaments are thicker in the thoracic region They are not paired structures with a midline cleavage as often described but rather like a single structure that extends from the roots of the articular process on one side to the corresponding process on the other (*Ramsey* 1966 *Gray* 1967) The ligament is composed of a large amount of elastic fibers (*Ramsey* 1966) and represents the most pure elastic tissue in the human body (*Braus* 1921) However *Ramsey* (1966) states that with aging there is a type of fibrous substitution which increases the relative amount of fibrous tissue *Akerblom* (1948) demonstrated elastic qualities of the yellow ligament from his investigation of the thoracolumbar spine He noted that the greatest degree of ventroflexion that could be achieved is that in which the interarcuate ligaments are stretched to a maximum He found that the interarcuate ligaments were the chief factor limiting ventroflexion in the freely dissected lumbar spine The ligament has been shown to have considerable active compressive force which prestresses the intervertebral disc (*Nachemson* and *Evans* 1968) These ligaments are also said to protect the disc by slowing flexion They are thought also to help restore the vertebral column to an erect attitude following flexion *Rolander* (1966) concluded that though the yellow ligament is probably the only ligament with restrictive activity such restriction is not a significant factor in the movement of the spine

The ligaments of the articular capsules are thin and loose Their attachment is just beyond the margins of the adjacent articular processes They are shorter and more taut in the thoracic and lumbar region than in the cervical region (*Gray* 1967) These ligaments do not become taut in ventroflexion before the

affect of the interarcuate ligaments are operative (*Åkerblom* 1948) The intertransverse ligaments pass between the transverse processes In the thoracic region they are characterized as rounded cords intimately connected with the deep muscles of the back The interspinous ligament takes its origin in the ligamentum nuchae and continues along the tips of the spinous processes as a round slender strand down to the sacrum This ligament is not as thick in the thoracic as in the lumbar or cervical region The supraspinous ligament has been observed to be taut on ventroflexion (*Åkerblom*, 1948 *Steindler* 1955) The length of the supraspinous ligament in the lumbar region in maximal ventroflexion is the same as the maximum length obtained with tensile stresses applied directly to the ligament This same phenomenon was noted in testing the interarcuate ligament (*Åkerblom*, 1948)

The ribs and the muscles are not involved in the scope of this investigation and consequently are not included in these anatomical considerations

CONSIDERATIONS TERMS AND DEFINITIONS

The following considerations are applicable to the remainder of this study Related concepts terms and definitions involving engineering mechanics are based on the texts of *Christie* (19[illegible]2) *Timoshenko* and *Young* (19[illegible]6) and *Shames* (1966)

The mechanics of the spine can be analysed intersegmentally as the motion of a rigid body (one vertebra) in relation to some reference (the subjacent vertebra) Precise description requires a coordinate system The system to be employed is a righthand Cartesian coordinate system which is fixed in each vertebra This reference system applies for the entirety of this work See Fig [illegible]

Motion of a rigid body is a combination of translation and rotation

Translation—A body is said to be in translation when movement is such that all particles in the body have at a given time the same velocity relevant to some reference

Rotation—A body is said to be in rotation when movement is such that all particles along some straight line in the body or a hypothetical extension of it have a zero velocity relative to some reference

Axis of Rotation—This is the line of stationary particles whose velocity is zero at the time of rotation

Coupling—This is applied to motion in which rotation about one axis is consistently associated with rotation about a second axis

From Fig [illegible] it can be seen that the planes can be defined as below

Sagittal—This is the x y plane

Frontal (coronal)—This is the y plane

Horizontal (transverse)—This is the x - plane

Flexion—This is movement predominantly in the sagittal plane ventrally directed (i e toward the negative direction of the x axis)

Extension—This is movement predominantly in the sagittal plane dorsally directed (i e toward the positive direction of the x axis)

Lateral bending (lateral flexion)—This is movement predominantly in the frontal plane to the right (toward the negative direction of the   axis) or to the left (toward the positive direction of the   axis)

Sagittal plane rotation—This is rotation about the   axis (θ) Positive θ is tilting forward as in flexion Negative θ is tilting backwards as in extension

Frontal plane rotation—This is rotation about the x axis (θx) Positive θx

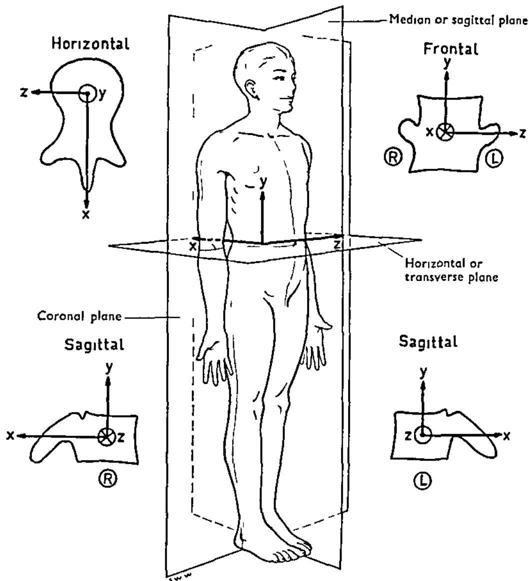


Fig 5 This shows the righthand Cartesian coordinate system to be used throughout this investigation The system is also indicated with views of a vertebra in the standard planes (The man and the body planes are reproduced from Gray's Anatomy 34th Edition London 1967 with permission of the publisher)

is tilting to the left as in left lateral bending and negative θx is tilting to the right in right lateral bending

Axial rotation—This is rotation about the y axis (θy) positive to the left (counterclockwise) Negative θy is rotation to the right (clockwise) Clockwise and counterclockwise are as viewed from above See horizontal view Fig 5

Thoracic (dorsal) *vertebrae* are numbered Th 1–Th 12

Motion segment—This is constituted by two vertebrae and their adjoining soft tissue (*Junghanns* 1931) The movement of a given vertebra unless otherwise stated is in relation to the subjacent vertebra

MOTION IN THE THORACIC SPINE

The following section is a review of the literature. It will be organized in such a way as to point up the basic considerations of importance in describing the motion of the thoracic spine. The inconsistances of previous authors are noted not to detract from their work but to illuminate the problems at hand. These previous studies have laid the more difficult ground work and they provided the foundation on which this and subsequent investigations can be developed. This review does not emphasize historical sequences or development of techniques. The history is thoroughly reviewed by *Elward* (1939) and *Inder on* and *Fl tr m* (1940). The technical development is described in the works of *I clinder* (1966) and *Lysell* (1969). The major topics in a description of the motion of the thoracic spine can be expressed by the questions heading each section of this review. These questions will constitute the outline for the review of previous investigations as well as the frame work on which the presentation of the material of this study is developed.

What is the Extent and Pattern of Flexion and Extension?

Weber (1827) was probably the first to actually do measurements of the motion of the vertebral spine. From his work based on the analysis of three cadaver spines he concluded that the majority of *the dorsal vertebra cannot be flexed but only rotated*. *Lovett* (1907) and *Elward* (1939) stated that *flexion is not great* and that *extension is very slight in the thoracic spine*. McKendrick in 1916 studied photos and made measurements of the spine in various attitudes. He observed and emphasized that there is *no flexion in the dorsal spine* (From *Keller* 1924). *Monro* (1966) based on roentgen studies in flexion and extension stated that *thoracic spine motion* under normal conditions and from a practical aspect is *almost nonexistant*.

Keller (1924) studied motion of the spine in living subjects by roentgenograms, electrical stimulation of the muscles of the thoracic spine and by careful measurement of markings on the skin. *He disagreed with the statement of immobility of the dorsal spine. The investigations were reported as showing segmental motion in flexion and extension* beginning with the 9th dorsal vertebra and moving caudally. He stated that the *upper portion has poor motion in the*

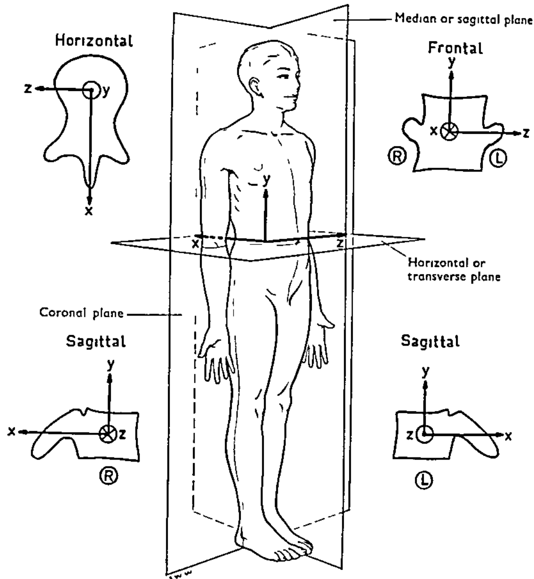


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The following section is a review of the literature It will be organized in such a way as to point up the basic considerations of importance in describing the motion of the thoracic spine The inconsistances of previous authors are noted not to detract from their work but to illuminate the problems at hand These previous studies have laid the more difficult ground work and they provided the foundation on which this and subsequent investigations can be developed This review does not emphasize historical sequences or development of techniques The history is thoroughly reviewed by *Eluard* (1939) and *Anderson and Ekstrom* (1940) The technical development is described in the works of *Polander* (1966) and *Lysell* (1969) The major topics in a description of the motion of the thoracic spine can be expressed by the questions heading each section of this review These questions will constitute the outline for the review of previous investigations as well as the frame work on which the presentation of the material of this study is developed

What is the Extent and Pattern of Flexion and Extension?

Weber (1827) was probably the first to actually do measurements of the motion of the vertebral spine From his work based on the analysis of three cadaver spines he concluded that the majority of *the dorsal vertebra cannot be flexed but only rotated* *Lovett* (1907) and *Elvard* (1939) stated that *flexion is not great* and that *extension is very slight in the thoracic spine* McKendrick in 1916 studied photos and made measurements of the spine in various attitudes He observed and emphasized that there *is no flexion in the dorsal spine* (From *Keller* 1924) *Monro* (1965) based on roentgen studies in flexion and extension stated that *thoracic spine motion* under normal *conditions* and from a practical aspect *is almost nonexistant*

Keller (1924) studied motion of the spine in living subjects by roentgenograms electrical stimulation of the muscles of the thoracic spine and by careful measurements of markings on the skin *He disagreed with the statement of immobility of the dorsal spine The investigations were reported as showing segmental motion in flexion and extension* beginning with the 9th dorsal vertebra and moving caudally He stated that the *upper portion has poor motion in the*

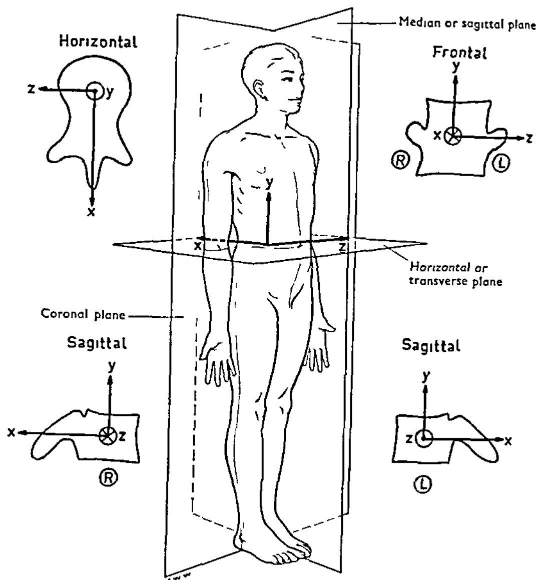


Fig 5 This shows the righthand Cartesian coordinate system to be used throughout this investigation The system is also indicated with views of a vertebra in the standard planes (The man and the body planes are reproduced from Gray's Anatomy 34th Edition London 1967 with permission of the publisher)

is tilting to the left as in left lateral bending and negative θx is tilting to the right in right lateral bending

Axial rotation—This is rotation about the y axis (θy) positive to the left (counterclockwise) Negative θy is rotation to the right (clockwise) Clockwise and counterclockwise are as viewed from above See horizontal view Fig 5

Thoracic (dorsal) *vertebrae* are numbered Th 1–Th 12

Motion segment—This is constituted by two vertebrae and their adjoining soft tissue (*Junghanns* 1931) The movement of a given vertebra unless otherwise stated is in relation to the subjacent vertebra

vertebra as totalling 52 25 *Lovett* (1905) studied cadavers and a live model whom he both selected and photographed carefully observing that *rotation in the dorsal spine gradually diminishes in a cephalocaudal direction* He accounted the following degrees of rotation from Th 1–Th 12 51 50 50 49 47 43 40° 34 27 25 21 17 *Steindler* (1955) wrote that rotation was 40 to either side *totalling 80* for the dorsal spine *Lindahl* (1962) reported about *3 –4* of axial rotation at each level of the dorsal spine *Gregersen* and *Lucas* (1967) inserted *Steinmann* pins in the spinous processes and conducted an in vivo investigation with seven subjects They too found a smaller quantity of motion than did *Lovett* (1905) They stated that there was a *total of 74 of rotation in the dorsal spine* with an average of about 6 at each level These writers noted that the *amount of rotation* in the upper portion of the thoracic spine *increases gradually from* Th7 upwards When their subjects were walking however the maximum rotation was observed at the middle portion of the thoracic spine

Is Rotation Coupled with Lateral Bending?

The issue of the presence or absence of a coupling of axial rotation with lateral bending has received the attention of a number of investigators (*Schulthess* 1902 *Lovett* 1905 1907 *Feiss* 1908 *Arkin* 1950 *Steindler* 1955 *Roaf* 1958 *Tidestrom* 1958 *Gregersen* and *Lucas* 1967) Here too there are differences of opinion *Roaf* (1958) studied the spines of stillborns and observed that *the two motions occurred independently* in the thoracic as well as in the lumbar regions *Lovett* (1905) studied cadaver spines and found *rotation and side bending to be inseperable* In the *erect* and the *hyper extended* positions he stated that the rotation was coupled with lateral bending He noted *it to be toward the concavity of the lateral curve* In other words when bending to the left the axial rotation of the vertebrae was also to the left However he reported that in the *flexed* position the axial rotation was *toward the convexity of the curve with lateral bending* To state it differently when the flexed thoracic spine was bent to the left the axial rotation of the vertebrae was to the right *Arkin* (1950) made roentgen investigations in 5 subjects and reported a *tendency for convex side rotation with lateral bending* in both the flexed and the extended positions *Feiss* (1908) and *Novogrodsky* (1911) also reported *rotation of the vertebral body to the convexity of the lateral curve* *Tidestrom* (1958) used a mechanical model of the spine to show that based on *Polhem* coupling *rotation is a necessary component* of side bending in the spine The direction of the rotation was not stated *Gregersen* and *Lucas* (1967) studied living subjects and found the *rotation* of the vertebral bodies with lateral bending to be *toward the concavity* of the curve

Table 1 gives an outline of previous descriptions of thoracic spine motion

anterior posterior plane *Balke* (1931) also published roentgen studies of vertebral motion He reported findings which differed widely with *those of previous* investigations describing segmental motion *Balke* described an *equal amount of flexibility at the various levels*

There is marked variation in reports regarding the total range of flexion and extension in the dorsal spine *Virchow* (1911) reported intersegmental motion of the thoracic spine When added they come to *108 0° total flexibility* in the sagittal plane between C7 and Th12 *Balke* (1931) found 45 9° extension and 22° flexion This constitutes a *total flexibility of 67 9°* with a ratio of approximately 2 1 extension vs flexion It is of interest to note that *Fick* (1904) reported *total flexibility* of the dorsal spine *of 135°* *Novogrodsky* (1911) studied four cadaver specimens and reported a *total of 62* for the intersegmental motion of the dorsal spine in flexion and extension

Loebl (1967) conducted in vivo measurements in 176 normal subjects using a special inclinometer and made recordings with the spine in various positions including full flexion and extension This is not intersegmental motion of course He reported his findings for total flexion and extension as far greater than is generally described He noted that the dorsal spine contributed about *25% of the total range of spinal movement in flexion and extension*

What is the Extent and the Pattern of Lateral Bending and Rotation?

According to *Keller* (1924) Mc Kendrick reported an *absence of lateral flexion* in the dorsal spine *Keller* (1924) wrote that there is *poor motion in lateral flexion* He also found the upper portion less mobile than the lower *Gray* (1967) stated that *lateral movement is free in any part of the column* *Lovett* (1905) stated that though the entire dorsal spine participates in lateral bending *the larger portion of such motion takes place below the 10th dorsal vertebra* In side bending in all positions he states that the 12th dorsal vertebra behaves as a lumbar vertebra *Lucas* and *Bressler* (1961) found *the most mobile elements to be between the 3rd and the 7th thoracic vertebra in lateral bending*

Novogrodsky (1911) reported a *total lateral flexibility of 76* *Balke* (1931) found about 2 –3° at each level for a *total of 30 6°* *Steindler* (1955) reported 30°–40° on either side or approximately *70 total*

A number of previous investigators agree that there is axial rotation in the thoracic spine (*Weber* 1827 *Hughes* 1892 *Keene* 1906 *Lovett* 1907, *Davis* 1918 *Keller* 1924 *Arkin* 1950 *Steindler* 1955 *Roaf* 1958 *Lindahl* 1962 *Gregersen* and *Lucas* 1967) Their statements disagree however on the amount of rotation its regional variation and the presence or absence of coupling of this motion with lateral bending

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vertebra as totalling 52.2°. Lovett (1905) studied cadavers and a live model whom he both selected and photographed carefully observing that *rotation in the dorsal spine gradually diminishes in a cephalocaudal direction*. He accounted the following degrees of rotation from Th 1–Th 12: 51°, 50°, 50°, 49°, 47°, 43°, 40°, 34°, 27°, 25°, 21°, 17°. *Steindler* (1955) wrote that rotation was 40° to either side *totalling 80°* for the dorsal spine. *Lindahl* (1962) reported about 3°–4° of axial rotation at each level of the dorsal spine. *Gregersen* and *Lucas* (1967) inserted *Steinmann* pins in the spinous processes and conducted an in vivo investigation with seven subjects. They too found a smaller quantity of motion than did *Lovett* (1905). They stated that there was a *total of 74° of rotation in the dorsal spine* with an average of about 6° at each level. These writers noted that the *amount of rotation* in the upper portion of the thoracic spine *increases gradually from* Th7 upwards. When their subjects were walking, however, the maximum rotation was observed at the middle portion of the thoracic spine.

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Table 1 Outline of Previous Descriptions of Thoracic Spine Mechanics

Author year	No of Subjects investigated	Method	Flexion and Extension	Lateral bending	Rotation	Coupling
Weber E H 18[illegible]7	3 cadavers 2 males 1 female live males age 20 [illegible]	Direct measurements	The majority of dorsal vertebrae cannot be flexed		Majority of dorsal vertebrae can only be rotated	
Hughes R W 189[illegible]	2 cadavers M age 20 M age 40	Attached metal pins to vertebrae studied movement in relation to subjacent vertebra			2nd thoracic to 1st lumbar 20 yr old 52 2[illegible]° 40 yr old 99 8 Lower portion moved less than upper	
Schulthess W 1902	Studied mechanical models			Pure side bending without rotation is impossible		Yes
Fick R 1904	1 cadaver	Direct measurement	Total flexibility 13[illegible]		Total amplitude 80	Yes to concavity of lateral curve
Lovett R W 190[illegible]	3 subjects cadavers 1 live ages [illegible]	Pins in spinous processes also photographed live model	Not an extensive motion for this part of the spine	Greatest in the mid dorsal region	The major motion of the spine is rotation	Yes Rotation to concavity of lateral curve In flexed position however rotation is to convexity
K[illegible] C W 1906	[illegible] cadaver 1 infant 1 adult M	Pins in spinous processes and tracings [illegible]			Can be effectively achieved by pressure applied to the appropriate corresponding ribs	

A th r Y a	N of S t ject t g t l	M th l	Fle on a l l t on	Lat al l n l g	R t t	Cou ling
N grol ky M 1911	4 M e laver fre h f m la preser l	St i h l l t r segment l t i th vertcl ae fitt l t n as i g apl rat i h ch n l e t l r t l l oa l l	l t thorn c to l t l uml ar 6	l t thorac e to l t l ml r total 1 76		Y s to con a ty of lat al c rve
V hov H 1911	l i laver	Pl t r cast ma le f sp c i 3 po i ti n in the f ll range f mot on in the ag ttal plane Po tion r gla ter a t w io tl n mea ured	T tal fl xib l ty lst th racic to the l t l uml ar 108 0			
Da G G 1918	Stat l i i t xtl k no experi nent lo cr l e l				I re in upper po t o of lor al reg on an l gradually l mini hes to absent n the l uml r regi n	
Kell r H A 19 4	1 male	X ray t t h s in vivo v tl careful k n i rking an l measur ments electrical st mula tion of mu cl s v th subj ts pron	Th e s p r motion n th upper regions i th a t or a l pc teri r l r ctions	P r moti n al o in lateral l rection th re is motion f m the 9th th oracic d n	Not l more rotat on in the upper portio i of thoracic sp n e	Yes to the concavity of the lat ral curve

Author year	No of Subjects investigated	Method	Flexion and Extension	Lateral bending	Rotation	Coupling
Bakke S N 1931	44 20 mal s 24 females ages 3–79	X ray investigation living subjects	There is an even grading of flexibility Total flexibility of thoracic spine 67 9 22 flexion and 45 9 extension	Equal amount of flexibility about 2–3 at each level total 30 6		
Steindler A 195_	Not stated	In vivo		Noted 30–40 to either side total approximately 70	Described 40 to either side for a total of 80 rotation in thoracic spine	Yes to the convexity of the lateral curve
Roaf R 19_8	2 fresh autopsy 1 infant 1 age 8	X ray studies also with pins as markers in spinous processes			Axes of rotation in region of posterior longi tudinal ligament	No
Tidestrom F 1958	Mechanical model	Constructed mechanical model of spine to describe mechanism of coupling		Based on same principal as Polhem coupling rotation is necessary		Yes
Lucas and Bresler 1961	3 frozen autopsy spec ag s 2_ 32 44	Spine with ligaments loaded and multiple rapid exposure photographs taken		Most flexible ele ments appear to be between the 3rd and 7th thor acic vertebrae		

Author year	No of Subjects investigated	Method	Flexion and Extension	Lateral bending	Rotation	Coupling
Davis and Troup 1965	13 ag s 18– 9	In vivo ch ono cyclophotogr ph c stu ly reflective trips o er p nou pro ess s	Very l ttle thoracic p te m tio with no defin te pattern			
Gregersen and Lu a 1967	7 ag s 0 6	In vivo vith St i man i pi s in the v t brae			6 at each level rotat ng fr m one xtre ie to the other 74 total fro 1st thorac c to 1 th thorac c The am unt ii cre ses gra lually from the th to the 1 t thoracic	1 to the concavity of the late al curve
Loebl W Y 1967	176 ages 15 84	I vivo i g n ncl o n ter	35 total for thora ic spine (not interseg mental t tal) The a nount was about of tot l flexion and extension for ntir sp ne			

Where are the Centers of Motion for the Various Movements?

The question of a center of motion or an axis of rotation has been discussed by various investigators in relation to movement of all regions of the vertebral column *Novogrodsky* (1911) considered the center of motion for combined lateral flexion and axial rotation to be somewhere in the anterior portion of the disc *Dittmar* (1930) demonstrated a *moving center of motion* in the *lumbar* spine *Elward* (1939) stated that there is *no single center of motion* *Gianturco* (1944) with roentgenologic studies of the *lumbar* spine observed *wide variation of the axis of motion* *Åkerblom* (1948) stated that the *center of motion was in the center of the disc* in the middle of the nucleus pulposus *Rockwell* (1938) suggested a theoretical center in axial rotation somewhere in the anterior portion of the vertebral body *Roaf* (1958) suggested that the *axis of rotation is somewhere in the region of the posterior longitudinal ligament* *Rolander* (1966) found a *large number of motion centers* with little or no regional clustering *Lysell* (1969) reported in his analysis of cervical spine movement that the *axis of rotation for flexion and extension was situated in the subjacent vertebra* It was not possible for him to state whether the axis of motion is fixed or is mobile He noted that in the combined motion of lateral bending and rotation there was very little movement of a measuring point in the anterior central portion of the moving vertebra From this observation he deduced that this point was very close to the center of motion

The broad variations in the description of thoracic spine motion noted in the preceding paragraphs is probably based on several factors The investigators employed different experimental methods Few subjects were analysed in most instances and the techniques of observation were rather imprecise There is variation of opinion on several points The extent of motion in flexion and extension and lateral bending does not seem to be at all agreed up The question of the presence or absence of coupling of lateral bending with axial rotation remains contraversial concerning both its existence and direction The descriptions of the regional variations within the thoracic spine are not consistant as regards each of these movements The questions of the existence and position of centers of motion and the possibility of their movement remain unsettled There is a paucity of information on the actual pattern of intersegmental motion

PART I

TWO DIMENSIONAL ANALYSIS WITH CONTROLLED LOADS

Method

Material

The material for these experiments was removed at the time of routine necropsy at one of the three following institutions University Hospitals Gothenburg Vasa Hospital Gothenburg and City Hospital Molndal The entire thoracic spine or some major portion of same was removed with a small portion of the attached ribs and the adjoining musculature Table 2 summerizes the relevant data on the subjects from which the material was removed There were 10 specimens in this part of the investigation The age range is 16 to 83 years Specimens with tumors fractures from patients with scoliosis and from patients with metabolic diseases known to affect bone were not included

Handling and Preparation of Test Material

A fresh specimen was received sealed in a plastic bag A roentgenogram was taken while the material remained sealed A motion segment for this part of the investigation was always made up of one of the following Th 1–2 Th 3–4

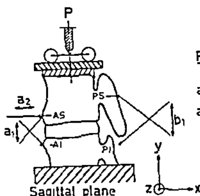
Table 2 Autopsy Material Part I

Subject	Years of Age	Sex	Cause of Death
IV	64	F	bronchopneumonia
V	71	F	respiratory and circulatory insufficiency
VI	83	F	arteriosclerosis with cerebral infarction
VII	57	F	rupture of basilar aneurysm
VIII	16	F	status epilepticus with [illegible] encephalitis
IX	33	F	diabetes mellitus with neuropathy
X	49	F	respiratory insufficiency
XI	46	M	myocardial infarction
XII	50	M	pulmonary edema
XIII	64	F	myocardial infarction

Th 5–6, Th 7–8, Th 9–10 or Th 11–12 On the basis of the *roentogengraph* and direct anatomical evaluation by the author the specimen was cut so as to include as many of the above defined motion segments as the material would allow (Due to damage or errors at the time of removal from the body the entire thoracic spine was not always usable) The remaining portion of the ribs were dissected away The muscles were removed and the ligaments preserved All soft tissue was removed from the superior one third of the more cephalad vertebrae and the inferior one third of the more caudad vertebrae of each motion segment This and all handling of the specimen unless otherwise stated was carried out in a specially constructed high humidity chamber This chamber maintained a relative humidity of 95% or greater The importance of maintaining a high humidity to preserve the physical properties of the annulus and the longitudinal ligaments has been well demonstrated by *Hirsch* and *Galante* (1967) *Galante* (1967) and *Tkaczuk* (1968) Specimens that were not to be analysed immediately were labeled sealed and preserved in a deep freeze at −25°C There is evidence that freeze storing does not affect the physical properties of bone (*Evans* 1957 *Sedlin* and *Hirsch* 1966) the annulus fibers of the disc (*Hirsch* and *Galante* 1967 *Galante* 1967) nor the ligamenta flava (*Åkerblom* 1948)

The motion segment(s) (MS) was prepared for testing as described below Those that had been stored by deep freeze were permitted to thaw overnight at +6°C while still sealed The unfrozen MS was treated as follows in the high humidity chamber The MS was balanced in a special metal tray so that the disc was horizontal with a flat level surface This sometimes necessitated removal of a portion of the more caudal spinous process The caudad member of the MS was fixed with a polyester cast (*Hirsch* 1964) Due to the marked vertical direction of the spinous process in the middle portion of the thoracic spine (Fig 2) it was sometimes necessary to remove the distal portion of the spinous process of the cephalad vertebra This was done so that the upper vertebra would not be fixed by the polyester A polyester cast was also constructed about the superior one third of the cephalad vertebra (Fig 10 No 5) This cast conformed to the general configuration of the vertebra and its top was horizontal and level (*checked with spirit level*) *When the polyester had* hardened the MS with the metal tray was sealed in a plastic bag and nails were affixed to the vertebra Two nails were placed anteriorly at each end of an *imaginary* vertical line 20 mm long The middle of this line was in the midline of the frontal plane of the vertebra and at approximately the middle of the height of the disc at that point This would be nails AS and AI shown on the sagittal plane of Fig 6 Nails PS and PI shown on the same diagram were placed in the spinous processes in the same *sagittal plane as nails* AS and AI and also vertical to each other Nails RS and RI were placed on the right side

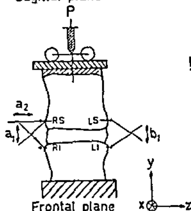
POSITION OF EXTENSOMETERS AND DISPLACEMENT GAUGES



Flexion and extension

a_1 and b_1 show rotation about z-axis

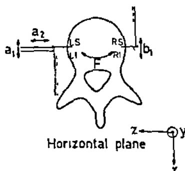
a_2 shows translation along x-axis



Lateral bending

a_1 and b_1 show rotation about x-axis

a_2 shows translation along z-axis



Rotation

a_1 and b_1 show rotation about y-axis

a_2 shows translation along z-axis

z y x

Displacement gauges

Extensometers

Nails

Fig 6 Diagrammatic representation of planes nails and motion gauges (P) is load (F) is moment The dashed lines represent nails and displacement gauges on the lower fixed vertebra See text for detailed explanation

Th 5–6 Th 7–8 Th 9–10 or Th 11–12 On the basis of the roentogengraph and direct anatomical evaluation by the author the specimen was cut so as to include as many of the above defined motion segments as the material would allow (Due to damage or errors at the time of removal from the body the entire thoracic spine was not always usable) The remaining portion of the ribs were dissected away The muscles were removed and the ligaments preserved All soft tissue was removed from the superior one third of the more cephalad vertebrae and the inferior one third of the more caudad vertebrae of each motion segment This and all handling of the specimen unless otherwise stated was carried out in a specially constructed high humidity chamber This chamber maintained a relative humidity of 95% or greater The importance of maintaining a high humidity to preserve the physical properties of the annulus and the longitudinal ligaments has been well demonstrated by *Hirsch* and *Galante* (1967) *Galante* (1967) and *Tkaczul* (1968) Specimens that were not to be analysed immediately were labeled sealed and preserved in a deep freeze at −25 C There is evidence that freeze storing does not affect the physical properties of bone (*Evans* 1957 *Sedlin* and *Hirsch* 1966) the annulus fibers of the disc (*Hirsch* and *Galante* 1967 *Galante* 1967) nor the ligamenta flava (*Åkerblom* 1948)

The motion segment(s) (MS) was prepared for testing as described below Those that had been stored by deep freeze were permitted to thaw overnight at +6 C while still sealed The unfrozen MS was treated as follows in the high humidity chamber The MS was balanced in a special metal tray so that the disc was horizontal with a flat level surface This sometimes necessitated removal of a portion of the more caudal spinous process The caudad member of the MS was fixed with a polyester cast (*Hirsch* 1964) Due to the marked vertical direction of the spinous process in the middle portion of the thoracic spine (Fig 2) it was sometimes necessary to remove the distal portion of the spinous process of the cephalad vertebra This was done so that the upper vertebra would not be fixed by the polyester A polyester cast was also constructed about the superior one third of the cephalad vertebra (Fig 10 No 5) This cast conformed to the general configuration of the vertebra and its top was horizontal and level (checked with spirit level) When the polyester had hardened the MS with the metal tray was sealed in a plastic bag and nails were affixed to the vertebra Two nails were placed anteriorly at each end of an imaginary vertical line 20 mm long The middle of this line was in the midline of the frontal plane of the vertebra and at approximately the middle of the height of the disc at that point This would be nails AS and AI shown on the sagittal plane of Fig 6 Nails PS and PI shown on the same diagram were placed in the spinous processes in the same sagittal plane as nail AS and AI and also vertical to each other Nails RS and RI were placed on the right side

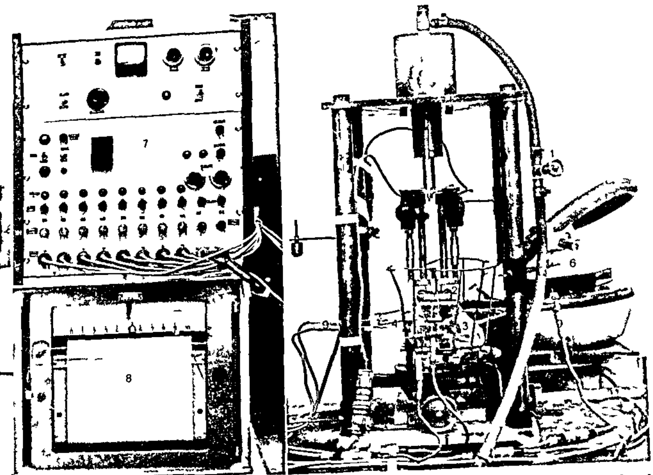


Fig Experimental Apparatus. To the right is the compression device (1) valve and air hose ( ) loading edge trolley and steel plate (3) specimen in plastic seal (4) displacement gauges (5) extensometer (6) humidifier and hose and (9) differential transformers. To the left is the (7) amplifier and channel selector and the (8) recorder

of the vertebra midway the anterior posterior diameter of the body. The nails both lie in the frontal plane and vertical to each other. Their heights corresponded approximately to those of the anterior nails AS and AI respectively. Positions of nails LS and LI had the same specifications but were placed on the left side of the vertebra. Nails RS, RI, LS and LI are shown in the frontal and horizontal planes of Fig. 6. Due to vertebral asymmetry and measuring error the above defined positions of the nails represent accurate approximations and not precise relationships. All nails were affixed through the plastic seal. The MS at this point was ready for analysis.

Experimental Apparatus

The experimental apparatus used in this part of the present investigation is the same equipment as was employed by *Hirsch* (1951), then subsequently modified and used by *Rolander* (1966). The same methods of calibrations and the same errors of measurement apply. The reader is referred to the latter reference for detailed description of the equipment and its use. The salient features of the testing material are summarized below. The equipment is photographed and shown in block diagram (Figs. 7 and 8).

The *compression apparatus* is designed so that a loading force of a known quantity, position and direction can be applied to the MS. The load is powered by compressed air. The amount and rate of application of the load can be controlled by standard valves. The load can be varied from 0–200 Kp and is recorded through electrodynamometers. A trolley resting on four ball races resting on a steel plate is placed between the loading edge and the top of the MS. This arrangement permits the specimen to rotate about some axis parallel to the loading edge and to translate along some axis perpendicular to it (Fig. 7, No. 2).

Movement of the specimens in the horizontal (*x z*) plane was recorded by *displacement gauges* (Fig. 7, No. 4). *Extensometers* (Fig. 7, No. 5) were used to record motion in the vertical planes sagittal (*y x*) and frontal (*y z*). In both cases motion is transformed into an electrical impulse created by the displacement of the antimagnetic stainless steel tip of a brass shaft inside an electromagnetic coil. This arrangement is called a *differential transformer* (Fig. 7, No. 9). There is an error of measurement inherent in any such motion gauge. In the case of the horizontal gauge, when the specimen rotates about its *z* axis (as an example see sagittal plane Fig. 6), the new position of the measuring point lies on the arch of a circle having a radius equal to the length of the measuring arm (approximately 80 mm). As the vertical displacement is ±2.5 mm the correction for the horizontal displacement is given by the sine of a very small angle. Consequently, it does not affect the recorded value. In

Poentgenograms were taken employing a portable *Schonander* machine with a 2 mm focus Those used for measuring were taken at a target to focus distance of 1 meter with about 10 cm between the center of the target and the film Poentgenographs were taken of a notched radiopaque measuring instrument at five positions in the 5 mm focus to film range in which the measuring points (nails) would be found The distance between the same two points represented on each of the five roentgen films was measured The mean of these measurements was taken The *actual* distance was then measured on the instrument The measurement on the radiograph was found to represent an 8 8% enlargement of the actual distance This information is employed in all calculations based on roentgenographic measurements under the above conditions

An Amsler *planimeter* was employed to measure the area of a tracing of the horizontally sectioned disc of each motion segment after testing was completed The accuracy of this instrument in the stated measurement was 0 10 cm

Procedure for Analysis of Motion Segments

The sealed MS with its nails in place and the lower vertebra fixed in the metal tray was attached firmly to a loading platform in the compression devise The MS was positioned so that its sagittal plane could be roentgenographed The platform was then rotated 90 and its frontal plane similarly pictured The horizontal displacement gauges and extensometers were then attached as indicated in Fig 6 (sagittal plane) The calibrations were checked By employing a scale on the compression devise (reading accuracy ±0 25 mm) and a pointer it was possible to make an accurate approximation of the diameter of the vertebral body in the sagittal and the frontal planes From these diameters the 25 50 and 75% positions shown in Fig 9 could be determined for the two planes These positions are employed in order to apply loads to the MS in such a way as to simulate the different movements of the spine They have the advantage of making comparisons of different motion segments more meaningful in that they have all been loaded at relatively the same points

The extensometers and horizontal displacement gauges were put into place to prepare the MS for testing The extensometers were held in position by rubber bands attached to an encircling brass cage The brass cage is also affixed to the loading platform By adjusting the tension and position of these rubber bands the extensometer could be balanced with its points positioned in shallow holes drilled in the previously described nails The horizontal gauges were similarly affixed to their appropriate nail heads with rubber bands All measuring points were derived from points on the specimen The extensometer itself recorded all vertical motion in relation to the subjacent vertebrae

BLOCK DIAGRAM

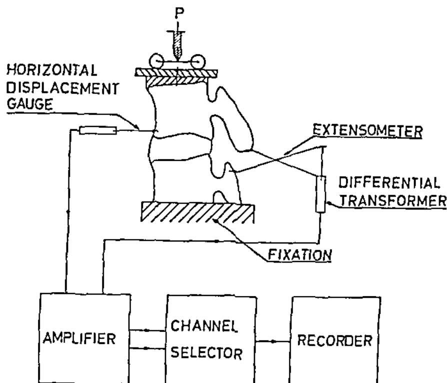


Fig 8 Diagrammatic representation of equipment (P) is load applied to motion segment

the case of the vertical motion gauge the horizontal displacement of the measuring point is along the arch of a circle with a radius equal to the distance between the tips of the gauges legs This distance is 25 mm ±5 mm Because of the relatively short radius for the vertical gauge there could be a large percentage of error in the vertical displacement if there was a large horizontal displacement The fact is however that the horizontal displacement has been quite small both in relative and absolute terms (*Rolander* 1966) Horizontal displacement was also very small in this investigation The median horizontal displacement for any given increment of force is estimated at 0 01 mm for this series

The information from the extensometers and displacement gauges was fed into a recording system This system included an *amplifier* a *channel selector* and a *recorder* (Figs 7 and 8) The reading error on the recorder was ±0 00› mm and ±0 1 Kp

An electrically driven *humidifier* with hose and a fiber glass horn at the end was employed Its purpose was to maintain a high humidity at that point in the procedure when it was necessary to disrupt the plastic seal

The forces to be applied were between 10–40 Kp 20–50 Kp and 30–70 Kp for the upper middle and lower two motion segments respectively The e ranges were selected so as to effect gradations of movement The intent was to apply enough of a load to assure significant motion but to avoid deformation of the bone At the same time the design was to select a range that could reasonably be assumed to include and exceed that of the superincumbent weight of the body This is discussed in more detail subsequently

The loading tests were conducted in the following manner The load was applied at the various positions 50 25 and 75% first in the sagittal plane then the MS was rotated 90 and the loads were applied in the three positions for the frontal plane For example Th 12 would be loaded in the sagittal plane at the 50 % position with 10 Kp followed by serial additions of 10 Kp to 20 30 40 and finally up to 50 Kp These increments and ranges of load were not followed precisely but served as guidelines However the precise load for each recorded movement of the specimen was indicated by the recorder After loading at the 50% position the subject was then similarly loaded at the 25 and the 75% positions Each series of loads at a given position was followed by a 5 minute pause for the residual deformation to pass The resultant position was then recorded Between the 25 and the 75% positions a very small external force (a light touch with a probe) was sometimes applied to move the specimen toward the initial starting position This resultant position was recorded and subsequent motion taken in relation to it

The rotation test was carried out as follows A threaded steel bar 4 mm in diameter and 17 cm long was pointed at one end This bar was drilled through the body of the superior (free) vertebra of the MS The bar was placed horizontal to the loading platform and in the upper one third of the vertebral body at approximately the middle of its anterior posterior diameter (Fig 10 No 1) A metal ring was secured between two ordinary nuts at either end of the bar The rings were positioned 4 5 cm from the respective entrance and exit of the bar into and out of the vertebra This positioning caused the lever arm of the moment and thus the force to vary directly with the frontal diameters of the vertebrae Each ring was wired to a cable which was fashioned to accomodate a series of measured weights at its distal end A system of pulleys was constructed which could be adjusted to correspond to the height and horizontal position of the attached end of the cable The cable was held perpendicular to the bar and in the same horizontal plane The pulley system could be adjusted to maintain these same conditions with the directions of the cables reversed Small grooves had been cut into the necks of the nails at positions LS LI RS and RI (Fig 6 horizontal plane) Specially constructed plexiglass connectors were employed They fit into the groove of the nail on one end and accepted the displacement gauge on the other This arrangement made it

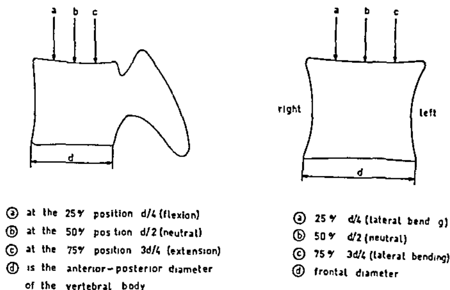


Fig 9 Diagram to show determination of loading position in sagittal and frontal planes See text for explanation

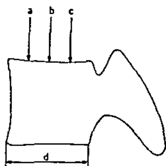
The *paired* horizontal displacement gauges provided information about relative horizontal motion between the vertebrae There were no external reference points With these conditions prevailing any extraneous motion of the compression apparatus could not affect the recorded information which represented the movement between the two vertebrae

The specimen was first pre stressed This variable was introduced to standardize the starting points and to minimise hysteresis *Virgin* (1951) stressed human intervertebral discs with the same load one minute apart He stated that it was conclusively demonstrated that the hysteresis during the second test was always appreciably less than during the first test In this study the pre stress load was applied at the 50% position of the sagittal plane Its *magnitude was 50 Kp for the upper two motion segments (i e Th 1–2 and* Th 3–4) 60 Kp for the middle two and 70 Kp for the lower two The load was applied five times A 5 minute interval was observed before the testing series began During preliminary experiments it was noted that most (>98%) of the residual deformation (hysteresis) passes in the first minute After 5 minutes all or nearly all had passed away Any remaining very small quantity could persist for several hours Because of this problem any residual deformation lasting more than five minutes was handled by either of two maneuvers depending on the dictates of the experiment It was either recorded and substracted from subsequent deformation or taken away by a slight external force These manipulations made all reading and consequently all motion comparable as far as the starting points were concerned

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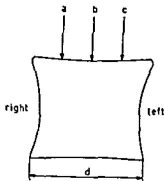


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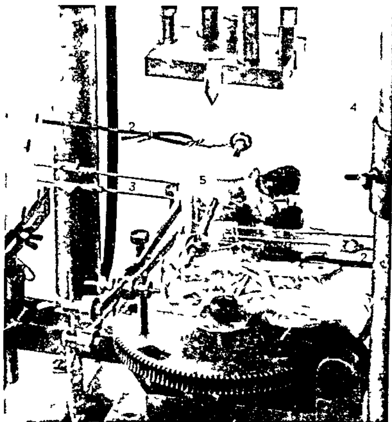


Fig 10 Photograph shows motion segment set up for testing *rotation* (1) metal pin in vertebral body (2) wires through which moment is applied (3) horizontal displacement gauges (4) horn from humidifier (5) polyester cast See text for explanation

possible to record motion in the horizontal (xz) plane (Fig 10 No 3) The axial rotation was then tested by adding measured weights of equal quantity to each cable after the pulleys had been adjusted as described above The initial load to each cable was 0 25 Kp The load was then increased on each cable by 0 5 Kp increments up to 1 75 or 2 25 Kp The cables were arranged to test the MS first in the counterclockwise direction ($+\theta y$) then in the clockwise direction ($-\theta y$)

An outline is provided to show the procedure as described above

I Schedule of Testing

A MS was pre stressed at the 50 % position in the sagittal plane

B Motion in the sagittal plane was tested

50 % position
25 % position—flexion ($+\theta$)
75 % position—extension ($-\theta$)

C Motion in the frontal plane was tested

50 % position

25 % position—bending to right ($-\theta x$)

75 % position—bending to left ($+\theta x$)

D Motion in the horizontal plane was tested

Counterclockwise	vertebral body turns to left ($+\theta y$)
Clockwise	vertebral body turns to right ($-\theta y$)

II Loads employed

A Loads for Sagittal and Frontal Testing

Pre stress		Range for Testing
Th 1–2 & Th 3–4	50 kp	10–50 kp
Th 5–6 & Th 7–8	60 kp	20–60 kp
Th 9–10 & Th 11–12	70 kp	30–70 kp

B Loads for Axial Rotation

2 75–30 05 kp cm

Range varied directly with frontal diameter of superior vertebra

In Fig 10 one can see two nails positioned at the side of the upper vertebrae The nails were placed along a vertical line perpendicular to the loading platform They were used to check with an additional extensometer (not shown in photograph) for deformation of the vertebra Several motion segments from different thoracic levels were arbitrarily selected and tested during the pre stress There was no indication of deformation In some instances loads up to 100 kp were applied without deformation During the routine testing of motion loads of such great magnitude were not employed Most probably for the range of stresses applied in this investigation the vertebrae behaved as rigid bodies

Removal of Posterior Elements

An additional experimental variable was introduced into the described routine The variable was introduced in order to compare in the same specimen under the same conditions the motion with and without the posterior elements It was felt that such comparisons would give some insight into the question of the role if any that these elements play in the mechanics of the thoracic spine For the purpose of this investigation the posterior elements (PE) shall be defined This term will be used to designate the following structures between any two vertebrae the facet joints the intertransverse ligaments the yellow ligament the inferior ½ of the laminae and the spinous process This leaves only the intervertebral disc and the anterior and posterior longitudinal ligaments connecting the two vertebrae

After the previously described manipulations were completed with the MS remaining in the apparatus the PE were removed The plastic seal was cut and with ordinary surgical instruments the task was accomplished without having to remove or even change the position of the MS Fig 10 shows a MS with this operation completed When the plastic seal is broken the humidifier (Fig 10 No 4) is directed on to the specimen in order to maintain a high humidity The MS is then loaded again exactly as when it was intact Thus the MS is tested in the same planes with the same range of loads at identical points of application

Data Processing Description and Comments

Five discretely increasing loads were applied to each MS at three positions in the frontal and sagittal planes first on the intact vertebra then with the PE removed There were eight to ten observations of rotation about the y axis resulting from discretely increasing moments on each MS with and without the PE As there were 50 motion segments this constituted close to 4 000 angles to be calculated from the raw data Computer analysis of the data was therefore employed using the following mathematical approach The rotation of a body in a plane can be determined by the movement of two points of the body in that plane The movement of the points in each of the three planes is represented by a_1 and b_1 in Figs 11 and 6 Fig 6 also explains how these values come from the measuring instruments The distance B_2 shown in Fig 11 is measured from a roentgenograph of the MS The 8 8 % magnification is corrected for during the computer analysis of the data The angle of rotation θ in a given

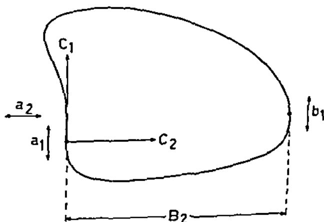


Fig 11 Diagram shows information needed to calculate angle of rotation and instantaneous axis of rotation of a rigid body rotating in one plane A point plotted on the coordinates C_1 and C_2 gives the location of the instantaneous axis of rotation for the body

roentgenographic plane can be calculated by the formular

$$\theta = [(b_1 - a_1)/B]$$

Information about horizontal movement is provided by a With the e in formations it is possible to calculate the position of the instantaneous axis of rotation that is the position on coordinates C_1 and C_2

$$C_1 = a_2/\theta$$
$$C = a_1/\theta$$

Cumulative force was plotted against cumulative displacement in angles for all MS in all planes of motion as shown in Figs 12 and 13 From the example given it can be readily observed that the points fit quite nicely to a straight line This visual observation is supported by statistical evaluation which employed the Method of least squares to test the extent to which the points fit a straight line Consequently it was possible to extract from the slopes meaningful approximations of the cumulative load and cumulative displacement in angles *between* the actual experimentally determined points A load of *6 Kp/cm²* and a moment of *20 Kp cm* were selected as the standard *forces to* be employed for extensive evaluation For this load and moment the cumulative displacement in angles of all the MS in all conditions of testing was extracted This additional analysis of the data was included to offer a meaningful comparison of the motion of a large number of MS from different subjects under conditions of a standardized force and constant relative point of application These extracted quantities of angle shall subsequently be *referred to as the* standardized motion(s) (SM)

There are several sources of error operative in the results obtained in this part of the analysis The errors can be divided into two *groups* namely those having to do with experimental factors and those related to the mathematical analysis *The* mathematical errors arise from the assumption that for the calculation of θ for small angles the movement of the points a_1 *and* b_1 represent movement along the arch of a circle This error was calculated for angl s *of* the quantities listed in Table 3 One is reminded that angles presented in the results are *cumulative* values The actual calculated *angles* that go to make up the cumulative values are *usually less than 3* Errors involved in the experimental method are difficult to generalize about as their influence varies tremendously in quantity and direction It is pos ible to be specific about such

Tabl 3 P rcentage of Errors in Cal ulated Angles

Cal ulated angle	1	3	5	8	10	1
P rcentage of rror	0 0[illegible]%	0 14%	0 39%	0 98%	1.04%	3 58 %

After the previously described manipulations were completed with the MS *remaining in the apparatus* the PE were removed The plastic seal was cut and with ordinary surgical instruments the task was accomplished without having to remove or even change the position of the MS Fig 10 shows a MS with this operation completed When the plastic seal is broken the humidifier (Fig *10 No 4) is directed on to the specimen in order to maintain a high humidity* The MS is then loaded again exactly as when it was intact Thus the MS is tested in the same planes with the same range of loads at identical points of application

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Five discretely increasing loads were applied to each MS at three positions in the frontal and sagittal planes first on the intact vertebra then with the PE removed There were eight to ten observations of rotation about the y axis resulting from discretely increasing moments on each MS with and without the PE As there were 50 motion segments this constituted close to 4 000 angles to be calculated from the raw data Computer analysis of the data was therefore employed using the following mathematical approach The rotation of a body in a plane can be determined by the movement of two points of the body in that plane The movement of the points in each of the three planes is represented by a_1 and b_1 in Figs 11 and 6 Fig 6 also explains how these values come from the measuring instruments The distance B_2 shown in Fig 11 is measured from a roentgenograph of the MS The 8 8% magnification is corrected for during the computer analysis of the data The angle of rotation θ in a given

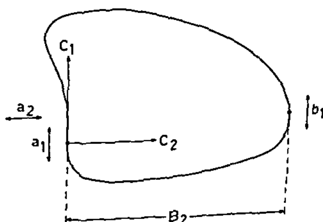


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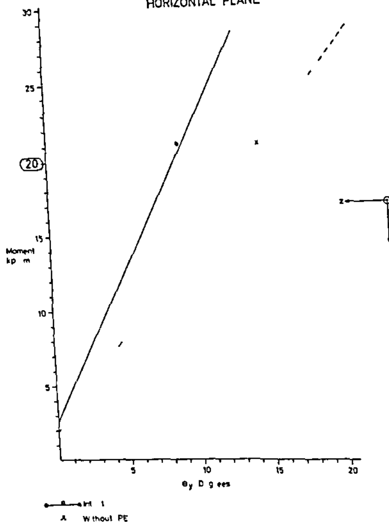
Results and Interpretation

The Effects of Various Loads and Moments on the Movement of the Motion Segments

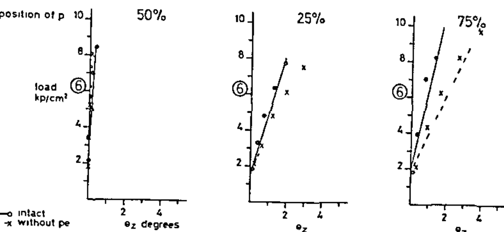
The data for all fifty MS was plotted as shown in Figs 12 and 13 This particular example is used because it is thoroughly representative In this section the motion referred to is rotation in all instances There was generally little or no motion when the MS was loaded at the 50% position This was the case for both the frontal and the horizontal plane In the sagittal plane there was generally more motion when the load was applied to simulate flexion of the movable vertebra (25% position) than when the load was applied to cause extension (75% position) In the experiments on axial rotation (θy) there was a pattern for the slopes of the force deflection curves They tended to increase as observations of the different MS were made in a cephalocaudal sequence See Fig 14 Table I in the Appendix gives the basis for statistical interpretation of differences in these slopes for all subjects The standardized motion of the various levels for the different subjects is given in Appendix Table II the means of the total motion in various experimental conditions is shown in Appendix Table III It is apparent that when flexion is simulated the movement is almost always greater than when extension is simulated If these two movements are combined the means of the combined sagittal motion can be seen to increase at the more caudal levels See Fig 15 Statistical evaluation of this trend gently supports this statement and its graphic representation at the 0 10 level of confidence Appendix Table IV gives the information for this statistical interpretation Similar evaluation of the SM in the frontal plane graphically and statistically implies more frontal motion at the lower MS when compared with the intermediate levels See Fig 16 and Appendix Table IV A comparison of the means of the SM in axial rotation at the different levels shows this motion to decrease as the observations move caudally Here again statistical analysis lends corroborative support with a 10% level of emphasis (Fig 17 Appendix Tables III and IV)

Based on this data certain statements can be made about the behavior of the thoracic spine MS when known forces are applied under controlled conditions Graphical and statistical analyses of the material show greater motion in flexion

errors only in a specific set of circumstances Some of the errors have been discussed Other errors are those having to do with the measurements of B_2 ($\pm 0\ 5$ mm) and the variations in the positions of the nails and extensometers To provide some guideline to the experimental errors a geometrical analysis and a mathematical estimate of the errors of a representative case were carried out The conditions were chosen so as to facilitate the effective operation of the errors This analysis estimates the maximum error of θ to be in the range of 3–4%



13 Graphic representation of cumulative moment and cumulative angles See text for explanation



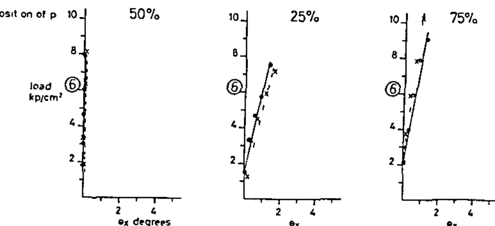


Fig 12 Graphic representation of cumulative load and cumulative motion in angles See text for explanation

than extension There is a definite tendency for greater flexion and extension at the lower levels as compared with the intermediate levels Motion in the frontal plane (lateral bending) shows also a tendency for larger quantities of movement at the lower MS when compared with the intermediate levels Axial rotation is greater in the upper levels and shows stepwise decrease as observations are made cephalocaudally

Effects of the Removal of the Posterior Elements

The behavior of the MS with the posterior elements removed is also recorded on Figs 12 and 13 and Appendix Tables II and III In the two dimensional

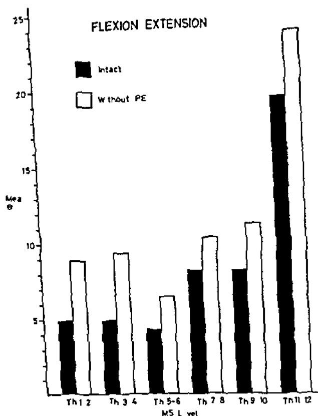


Fig. 15 Graphic representation of means of standardized motion of combined flexion and extension at the different vertebral levels with and without the posterior elements See text for description

was employed on the hypothesis that the mean difference with and without the PE is zero (*Brownlee* 1965) This test was carried out for all the types of motion described except that at the 50 % position in the frontal and sagittal planes Statistically significant differences were noted in the slopes after removal of the PE at the 75° position in the sagittal plane and with the tests for axial rotation These differences were significant at the 0 05 level of confidence and in the positive direction for the cumulative angle values In other words graphic and statistical analysis of the data shows that with removal of the PE there is a greater motion per unit force when such force is applied to simulate extension and axial rotation

The standardized motion (SM) was also studied to recognize any effects of the elimination of the PE Here too the differences were evaluated by the

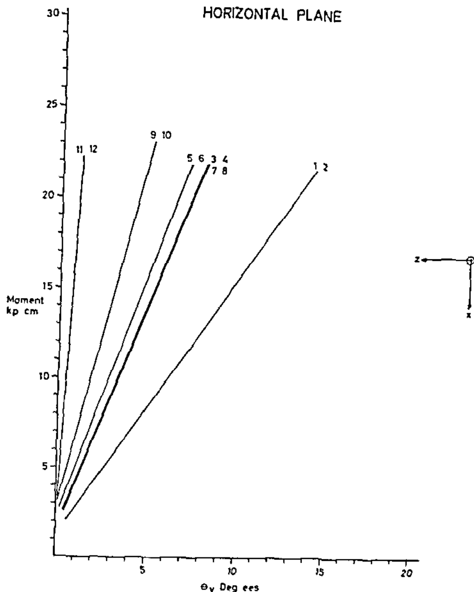
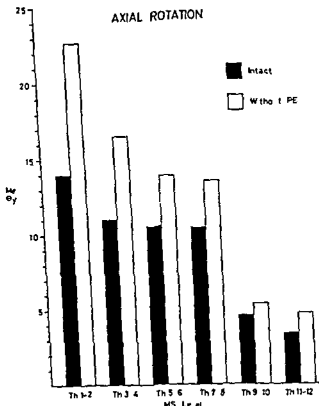


Fig 14 Comparison of slopes for cumulative moment and cumulative motion in angles for different vertebral levels in one subject See text for discussion

studies it can be said that removal of the PE effected significantly the motion in several parameters Visual evaluation of the slopes as seen in Fig 12 reveals slopes of a more acute angle with the horizontal at the 25 % and 75 % positions in the sagittal plane after removal of the PE Furthermore, the slopes were shifted toward a higher range of cumulative angle values This general trend could be observed as an over all trend by inspection of the other 40 graphs like Fig 12 The same generalization characterizes *the change in axial rotation* demonstrated in Fig 13 Statistical analysis was carried out The Sign test



F g 17 Graphic representat on of m ans of standardized motion of axial rotation at the iff rent vertebral l vel with and w thout the posterior elements See text for description

proces ing took into account radiologic magnification and adjusted the C_1&C_2 calculations to make the location of the IAP correspond accurately to the image on the film

Fig 18 shows representative examples of the IAR in the sagittal plane The majority of the MS showed clustering of the points within a 5 mm diameter circle In all instances the axes for exten ion were located above those for flexion Those for exten ion were located above the di c and more anteriorly while those for flexion were found below the di c and posterior to the extension axes In a small minority of examples the axes for extension were above the body of the moving vertebrae This can be seen in subject VIII Th 5-6 Fig 18 When the posterior elements were removed the IAR generally remained clu tered and moved only a small di tance away from the corresponding points for the intact vertebrae (ubject IX Th 9-10 Fig 18) The representa

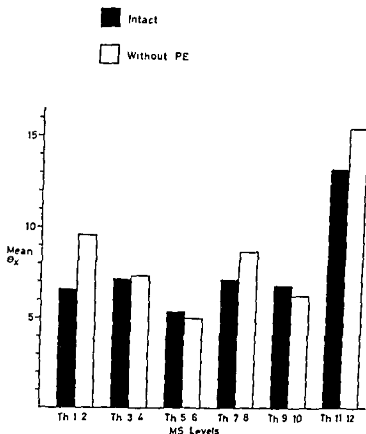


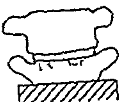
Fig 16 Graphic representation of means of standardized motion of combined lateral bending at the different vertebral levels with and without the posterior element See text for description

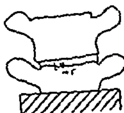
Sign test In these observations differences were noted at the 25% and 75% positions in the sagittal plane and with axial rotation These differences again are in the direction of an increase of motion and they are significant at the 0 05 level of confidence Figs 15 16 and 17 show graphically all the differences in the amount of motion in the various planes with and without the posterior elements

Instantaneous Axes of Rotation

Calculations of the instantaneous axes of rotation (IAR) were carried out and plotted on tracings of the corresponding radiographic views of all the motion segments of the three youngest and one of the older subjects Data

TWO DIMENSIONAL ANALYSIS OF INSTANTANEOUS AXES OF ROTATION IN FRONTAL PLANE OF ROENTGENOGRAM





R



L





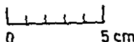
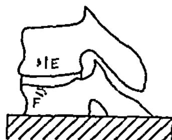
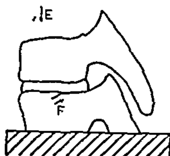


Fig 19 Examples of instantaneous axes of rotation (l) indicates the axes when vertebra was loaded at the [illegible] position (left lateral bending) (r) indicates the axes when the vertebra was loaded at the [illegible] position (right lateral bending) The circles show the corresponding IAR after the posterior elements were removed The diagrams represent actual tracings from roentgenograms. See text for further description

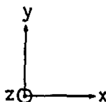
TWO DIMENSIONAL ANALYSIS OF INSTANTANEOUS AXES OF ROTATION IN SAGITTAL PLANE OF ROENTGENOGRAM

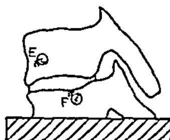


Subj IX Th 3-4



Subj VIII Th 5 6





Subj IX Th 9 10



Subj IV Th 11 12

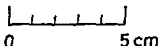


Fig 18 Examples of instantaneous axes of rotation (E) indicates the axes when vertebra was loaded at the 75% *position (extension)* (F) indicates the axes when vertebra was loaded at the 25% position (flexion) The circles show the corresponding IAR after the posterior elements were removed The diagrams represent actual tracings from roentgenograms *See text for further description*

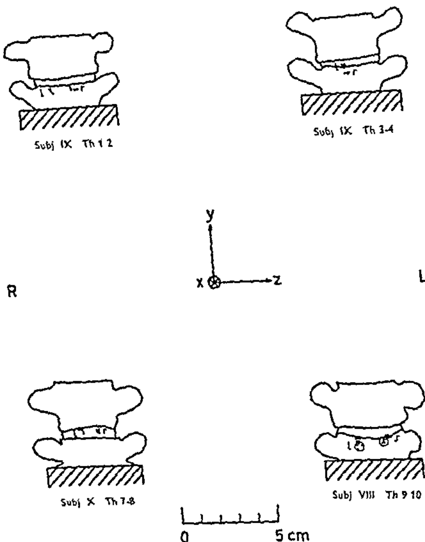
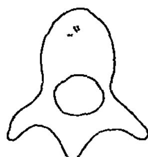
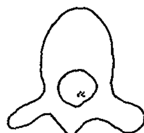


Fig. 10 Examples of instantaneous axes of rotation (l) indicates the axes when vertebra was loaded at the 75 position (left lateral bending) (r) indicates the axes when the vertebra was loaded at the % position (right lateral bending) The circles show the corresponding IAR after the posterior elements were removed. The diagrams represent actual tracings from roentgenograms. See text for further description

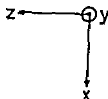
TWO DIMENSIONAL ANALYSIS
OF INSTANTANEOUS AXES OF ROTATION
IN HORIZONTAL PLANE OF ROENTGENOGRAM

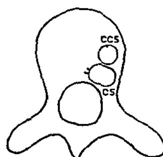


Subj XII Th 5 6



Subj XIII Th 7 8





Subj XII Th 9 10



Subj XII Th 11 12



Fig 20 Examples of instantaneous axes of rotation (c) indicates those axes when rotation was clockwise (cc) indicates those axes when rotation was counterclockwise (cs and ccs) *show the same without the posterior elements* The diagrams represent actual tracings from roentgenograms See text for further description

tive examples of IAR for the frontal plane are depicted in Fig 19 Here as in the sagittal plane there was clustering of the points On left lateral bending (positive rotation about the x axes) the IAR tended to cluster to the right of the midline Conversely with right lateral bending (negative rotation about the x axes) the IAR were observed to be to the left of the midline This pattern was evident in the data presented by *Rolander* (1966) with movement of the lumbar spine in the frontal plane Again ablation of the posterior elements resulted in only minimal movement of the still clustered IAR (Fig 19 subject VIII Th 9–10)

The IAR in the horizontal plane during axial rotation has been calculated and depicted in the same manner in Fig 20 All motion segments for subjects XII and XIII were analysed It should be mentioned that for technical reasons these points are not considered to be entirely as accurate as for the preceding two planes Rotation was tested in two segments counterclockwise then clockwise and generally the points were clustered The groups of IAR tended to be in the midline at different points along the x axis Removal of the posterior elements resulted in a somewhat greater shift here than was noted in the preceding two planes (Fig 20 subject XII Th 11–12) These observations seem to fit with the movement of *Davis* (1959) intersection point and the suggestions by other writers that the orientation of the plane of the facet joints influence the axis of axial rotation (*Pockwell* 1938 *Gregerson & Lucas* 1967) The IAR were not found as far anteriorly in the vertebral body as where *Lysell* (1969) suggested the possible center of axial rotation in the cervical spine might be located

Age and Motion

The experimental control of applying loads at relatively the same positions (0 25 and 75% of the diameter in the plane in which motion was tested) allowed a comparison between different subjects The total SM in the sagittal and frontal planes was combined for the Th 7–8 MS of each subject and plotted against age in years Similarly total rotation at the same MS (Th 7–8) for each subject was plotted Inspection of Figs 21 and 22 shows that there is no evidence in this data of any relation hip between amount of motion and age of subject This wa the ca e for axial rotation as well as for the total motion in the sagittal and frontal planes

Motion ratio and Total Motion

It has been suggested that the amount of allowable motion at a given intervertebral segment may be related to the amount of di c material and the diameter of the vertebral body in the plane in which the predominant motion

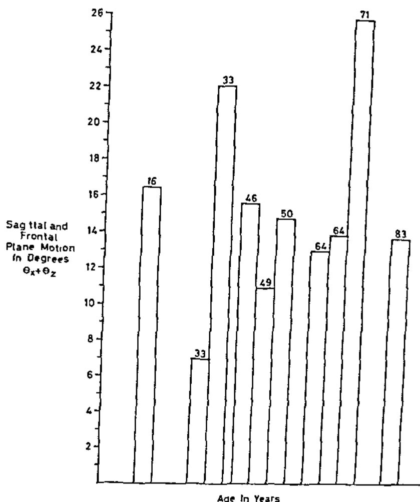


Fig 21 Graph shows total motion (combined sagittal and frontal planes) for Th 7-8 of each subject as related to age of subject See text for discussion

takes place (*Fick* 1904 *Keller* 1924 *Wiles* 1935 *Lucas* and *Bressler* 1961) In evaluating this hypothesis it was possible to make further use of the experimental controls employed and look at the SM as related to the disc heights and diameters For all the motion segments the disc height was measured on roentgenogram at three points the anterior middle and posterior regions of its diameter in their sagittal views and the right middle and left regions in their frontal views An average of each set of three values was taken as the disc height The disc diameter was then measured on roentgenograph in the two

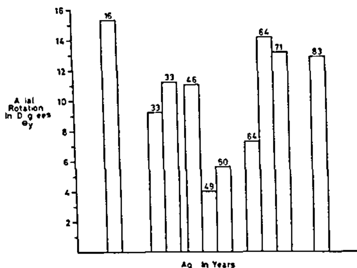


Fig Graph shows the amount of ax al rotat on of Th 7–8 of each subject as related to age of subject See text for discussion

planes The disc height/disc diameter ratio was calculated for each MS in the frontal and sagittal roentgenographic planes This ratio of disc height/disc diameter is what is meant by motion ratio

In order to test the hypothesis that an increase in motion ratio is correlated with an increase of motion the Th 7–8 MS for all subjects was selected A ranking of the motion ratio for Th 7–8 of each subject revealed almost no tendency for correlation This was the case for motion in both the frontal and the sagittal planes with or without ablation of the posterior elements See Table V in Appendix

Comments

Certain considerations are relevant regarding the interpretation of the findings in this part of the investigation In an analytical study of a mechanical nature it is important to have information about force and deformation When such information is analysed it is possible to recognize any constant relationship between the two variables and make predictions about one based on a knowledge of the other and the constant In engineering terms this straight line relationship between force and deformation (rotation in angles) is characterized by a *spring constant* This is represented by the slope of the line plotted in Fig 23 and for all the data as shown in the exemplary Figs 12 and 13

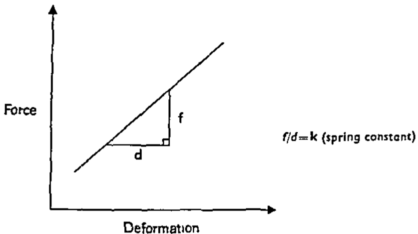


Fig 23 See text for explanation

It has been shown previously that for the range of forces involved in this experiment the cumulative forces and angles of rotation strongly tend to form a straight line relationship Thus it can be stated that in this series for the forces employed the MS behaved in a manner that can be analysed in mechanical terms of a spring constant

The range of the loads employed in this study in relation to some gross estimates of the loads imposed by gravity at the various thoracic vertebral levels has been considered These are given in Table 4 The calculations are

based on the estimated percentages of body weight above different vertebral levels (*Ruff* 1950 *Hensel* et al 1968) applied here to the perennial hypo

Table 4 Estimates of Superincumbent Body Weight of a Hypothetical Subject and Experimental Load Ranges at Various Levels

Vertebral Level	% of Superincumbent Body Weight	Weight in Hypothetical 70 kg Subject	Hypothetical Load Kp/cm²	Ranges of Experimental Loads Kp/cm²
Th1	9%	6.3 kg	1.4	[illegible]–10.8
Th8	33%	[illegible]3 kg	[illegible].7	2.4–7.2
Th12	47%	33 kg	[illegible].3	[illegible]1–5.0

thetical 70 kg man In order to estimate the area of the vertebrae at the different levels the average area for the corresponding level found in this investigation was employed The experimental load range was arrived at by dividing the Kp load range used in this experiment for the different levels by the average area of the vertebrae for that level The lower portion of the experimental range is close to or within the range of the estimated load imposed by the approximated superincumbent body weight Estimations of the loads involved during the characteristic movements of the living thoracic spine would be extremely difficult Nevertheless it appears that the selected force of 6 Kp/cm² is probably a good deal greater than the gravitational forces A relatively high moment 20 Kp cm was chosen to observe rotation In both instances a relatively strong force was employed in order to bring out the cephalocaudal differences and the intact compared with the ablated PE differences The knowledge and control of the forces made possible meaningful and reliable interpretations of the observed differences

Several generalizations regarding cephalocaudal variations seem reasonable based on this series The lower portions of the thoracic spine behaved more like the lumbar spine than did the *middle portion* This was apparent in two characteristics (1) greater motion in the sagittal plane (2) less motion in the horizontal plane (axial rotation) The vertebrae in the central portion tended to behave as a homogenous group In lateral bending tests no salient pattern of variation at the different levels *emerged*

Removal of the posterior elements resulted in *greater motion* in flexion in extension and in axial rotation This information has direct clinical applicability as regards traumatic and surgical involvement of these structures Two dimensional analysis of *the motion of these* segments in the frontal and sagittal planes of their *roentgenographic* projections provide *clinically* useful

information While the surgeon is of course thinking always in three dimensions the actual pictures before him are usually those of frontal and sagittal roentgenograms Therefore, if he keeps in mind that the two dimensional analysis is a simplification of the true motion the information described here can be effectively utilized in clinical evaluations

PART II

THREE DIMENSIONAL ANALYSIS

Method

Material

The sources of the specimens are the same as for those employed in part I of this study Table 5 summarizes the relevant data on the specimens used in this part of the investigation There were 17 subjects Their ages ranged from 5 to 83 years Specimens with tumors fractures from patients with scoliosis and from patients with metabolic diseases known to affect bone were also excluded from this group

Table 5 Autopsy Material Part II

Subject	Years of Age	Sex	Cause of Death
1	84	M	pulmonary edema
	41	F	hemmorage of external iliac artery
3	44	F	uremia
4	8	M	cerebral vascular insufficiency
5	49	M	diabetic nephrosclerosis
6	4	F	ovarian carcinoma
7	57	F	bronch pneumonia
8		F	chronic pulmonary disease with circulatory insufficiency
9	55	M	hypernephroma pneumonia
10	36	M	bilateral pulmonary emboli
11	16	F	respiratory insufficiency by suspension (suicide)
12	57	M	cerebral vascular insufficiency
13	[illegible]	F	fatty degeneration of liver
14	18	M	congenital heart disease
15	16	M	suffocation by drowning
19	5	M	post traumatic intra abdominal hemmorage
20	[illegible]	M	cerebral contusions

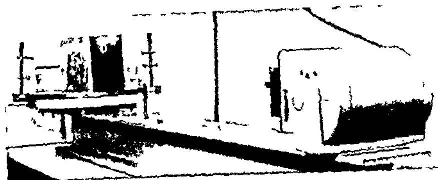
Handling and Preparation of Test Material

As in Part I of this investigation the specimens were protected from physical changes by storing in a deep freeze When working with the specimen it was always sealed in a plastic bag or kept in the high humidity chamber A roentgenogram of the specimen was taken in its sagittal and frontal planes Based on the roentgenograph and anatomical evaluation it was cut so as to preserve either the upper or lower 6 or 8 vertebrae for testing The roentgen apparatus could not accomodate any larger segment of the adult thoracic spine It was possible to test much larger portions of the small 5 year old spines The thawed specimen was handled in the following manner The ribs were dissected away The majority of the para spinous muscle mass was removed leaving a small amount of muscle tissue as an additional protective seal against dehydration of the deeper structures Four 0 8 mm steel balls were inserted into each vertebra The anterior ball (A) was inserted in the midline of the anterior portion of the vertebral body a few millimeters below the upper end plate and just beneath the cortex The posterior one (P) was similarly inserted at the base of the spinous process as close as possible to the midline sagittal plane The remaining two balls R and L were also inserted subcortically but at the right and left side of the vertebral body and slightly posterior to the middle of its anterior posterior diameter The preparation was then fixed in a brass cup by at least one vertebra held with polyester of the type described in Part I of this work The brass cup was specially constructed to fit into the roentgen apparatus The specimen and cup were placed in a plastic bag A hook was attached to the uppermost vertebra by screwing it into the cancellous bone of the body The specimen was then ready for examination

Apparatus and Experimental Technique

As stated previously the technique and apparatus for this portion of the investigation is the same as that used by *Lysell* (1969) A more detailed description is available in that thesis To follow is enough detail to provide the reader with a basic understanding of the technique without having to actually search the above work

See Fig 24 This equipment is constructed so that the object Table (A) is circular and can rotate about a vertical axis which runs through a reference point (R) (R) is a steel ball 8 mm in diameter placed in a pillar of plexiglass The object table can be locked in several positions For this study +22 5 (pos I) and −22 5 (pos II) were employed A roentgen film holder (B) lies behind the reference point and perpendicular to the rotation plane of the object table The film holder can be displaced parallel to the T square ruler (C) The front of the film holder is perforated and can be attached to a



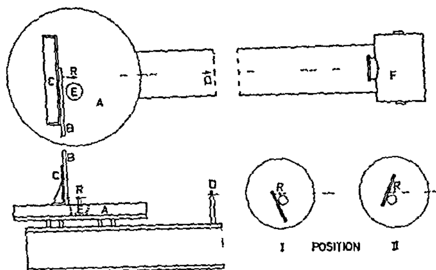


Fig. 24 Roentgen apparatus. For description see text

vacuum. This makes it possible to secure an uncovered roentgen film fixed flat against the holder. The position where the brass cup which holds the specimen is located is represented by F. Between the roentgen tube and the object table there is a metal rod (D) which has a hole in its flattened top. The position of this hole is such that an imaginary line drawn through its center and the center of the reference point is parallel with the rotation plane of the object table. The described line is also perpendicular to the axis of rotation and to the film plane in position 0 (the middle position between positions I and II). Before measuring the tube is adjusted and fixed so that the reference point is projected in the center of the projected hole (of the metal rod) onto the roentgen film. With this adjustment it follows that a roentgen beam from the focus through the reference point strikes the film perpendicularly if it is in position 0

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During the actual taking of the roentgenographs of the specimens the object table is first turned to position I (Fig 25 A) The film holder is moved to the left and the left part of the film is covered with a roentgen opaque shield The exposure for this position can be made The object table is now rotated 45 to position II (Fig 25 B) The film holder is displaced to the right and the right part of the film is covered Now the second exposure can be made Considerable care is taken not to alter in the least either the position of the specimen or the position of the film on the holder during the time between the two exposures

The geometry the mathematical analysis employed and the method of measuring on the radiographs are exactly as described on pages 23–28 in the thesis by *Lysell* (1969) Only the coordinate system is different in this investigation

Manipulation of Specimen

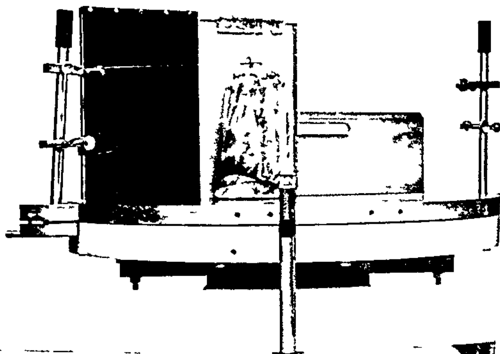
The specimen was moved in flexion and extension and lateral bending by attaching thin metal wires to the previously described hook in the uppermost vertebra See Fig 26 Nine exposures were taken of motion in the sagittal plane starting with full extension and ending with full flexion Three of these exposures were to the extension side of the resting position (Pe) (position of spine with no external load applied) An exposure of the Pe was made along with more to the flexion side of the Re Motion in the frontal plane totalled seven exposures three on either side of the Re and the Pe itself This movement was started with full right lateral bending and ended with full left lateral bending Axial rotation was taken from complete counter clockwise rotation to complete clockwise rotation in seven steps with three on either side of the Pe and including the Pe This maneuver was made possible by drilling a stainless steel pin through the body of the uppermost vertebra Through a specially constructed metal fork which could be attached to this pin the rotary force could be applied

The end points for the full range of these motions was readily recognizable by this investigator At the extremes of the ranges there is a gradually increasing moderate resistance followed by a distinct abrupt rapidly increasing strong resistance This latter very narrow range of resistance was taken as the end point for the total ranges in these experiments

Data Processing Description and Comments

The data from this portion of the study was analysed by two approaches From the primary measuring points on the radiograms it was possible to obtain precise information about the position in space of each of the 4 steel balls placed in each vertebra Mathematical computation included calculation of

I A



II B

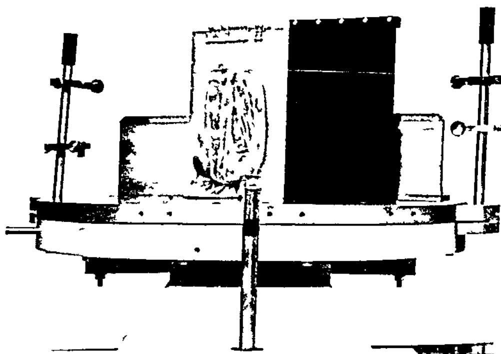


Fig 25 Object table with mounted specimen in position I(A) and position II(B) Pictures are taken from focus of roentgen tube

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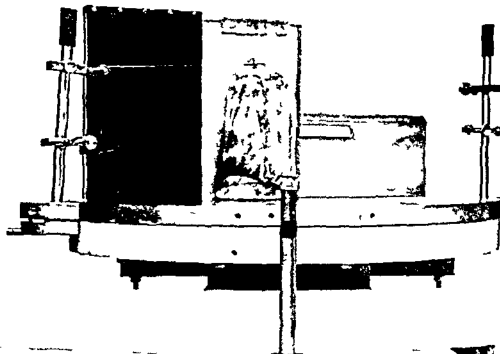
Manipulation of Specimen

The specimen was moved in flexion and extension and lateral bending by attaching thin metal wires to the previously described hook in the uppermost vertebra See Fig 26 Nine exposures were taken of motion in the sagittal plane starting with full extension and ending with full flexion Three of these exposures were to the extension side of the resting position (Pe) (position of spine with no external load applied) An exposure of the Pe was made along with 5 more to the flexion side of the Re Motion in the frontal plane totalled seven exposures three on either side of the Re and the Re itself This movement was started with full right lateral bending and ended with full left lateral bending Axial rotation was taken from complete counter clockwise rotation to complete clockwise rotation in seven steps with three on either side of the Re and including the Re This maneuver was made possible by drilling a stainless steel pin through the body of the uppermost vertebra Through a specially constructed metal fork which could be attached to this pin the rotary force could be applied

The end points for the full range of these motions was readily recognizable by this investigator At the extremes of the ranges there is a gradually increasing moderate resistance followed by a distinct abrupt rapidly increasing strong resistance This latter very narrow range of resistance was taken as the end point for the total ranges in these experiments

Data Processing Description and Comments

The data from this portion of the study was analysed by two approaches From the primary measuring points on the radiograms it was possible to obtain precise information about the position in space of each of the 4 steel balls placed in each vertebra Mathematical computation included calculation of



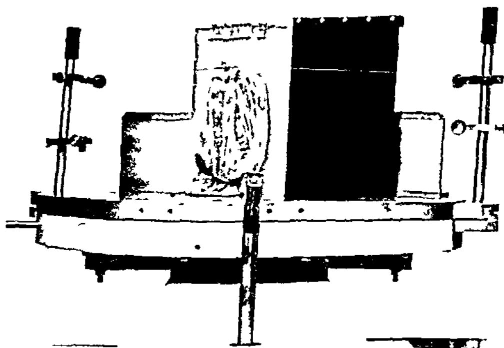


Fig 25 Object table with mounted specimen in position I(A) and position II(B) Pictures are taken from focus of roentgen tube

Results and Interpretation

The Pattern of Motion

The 5th thoracic vertebrae of subject 3 was selected to demonstrate the pattern of motion for it is thoroughly representative both qualitatively and quantitatively. Its pattern of motion is depicted in Figs 27, 28 and 29. One will note immediately that there is very little motion. This is perhaps a salient characteristic of the movement of the thoracic spine.

Sagittal motion is depicted in Fig 27. Looking at the x–y plane, the relative motion can be defined as translation in the negative direction of the x axis and rotation in the positive direction about the axis. The dashed line connects the A and P points in the position of full extension. In the neutral or resting position they are connected by the uninterrupted line. The position of full flexion is indicated by the point dashed line. The range of extension can be seen to represent about 1/3 of the total range. The movement of points R and L in Fig 27 is over simplified due to the limitation of space in which to represent it.

The view of this motion is shown again on the same figure in the x–z plane. The subjacent reference vertebra 6 is not shown on this view. In this plane the predominant motion one notes is translation along the x axis.

The pattern of motion in lateral bending is shown in Fig 28. A study of these diagrams shows that in motion from full right lateral bending to full left lateral bending there is translation along the axis in the positive direction and rotation about the x axis in the positive direction. There is also a rotation about the y axis in the positive direction. This is seen best in the horizontal (x–) view. However, it can also be observed by a study of the motion of points A and I in the frontal (y–) view. In different terms it can be stated that in this example *with lateral bending the vertebra rotates into the concavity of the lateral curve*. There is coupling of rotation about the x and y axes with directions positive about both axes. *Lysell* (1969) found such motions to be strongly coupled and in the same directions in the cervical spine.

Axial rotation is patterned in Fig 29. The specimen is taken from a full counterclockwise to a full clockwise position. The coupling of rotation about the

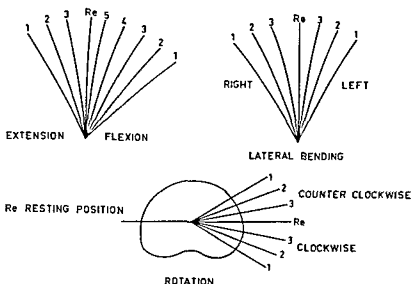


Fig 26 Diagrammatic representation of steps within ranges of motion studied See text for explanation

numerical vectoral quantities of the relative positions of the secondary measuring points A P R and L in adjacent vertebrae Secondary measuring points are mathematically determined points which facilitate the study of relative motion by establishing symmetrical and comparable neutral positions (*Lysell* 1969) Thus it was possible to plot the positions of these points in relation to the subjacent vertebra at various steps within the total range of movement in the sagittal frontal and horizontal planes Points were plotted from all the subjects in the three planes of motion It is from this analysis that it was possible to determine the actual *patterns* of motion

The second portion of the data analysis begins with the positions of A P and L on the x y and z coordinates in relation to the reference point (R) Calculations are made of a number of different informations to be reported and discussed in the following section of this investigation Even though the experimental error is small it proved to be out of the range of precision necessary for standard available mathematical approaches Consequently a special system had to be devised one that would allow for the experimental error and still provide a true three dimensional analysis of the motion Mathematical evaluation of the amount of the resultant error has found it to be 4 % for angles of 5 and 8 % for angles of 10

The mathematics were worked out in cooperation with a mechanical engineer The details and the theoretical basis of this analysis is to be published in a separate work (*Panjabi* and *White* 1969)

From the 17 subjects included in this part of the study the motion of 141 vertebrae was analysed by two programs producing 219 000 informations

Results and Interpretation

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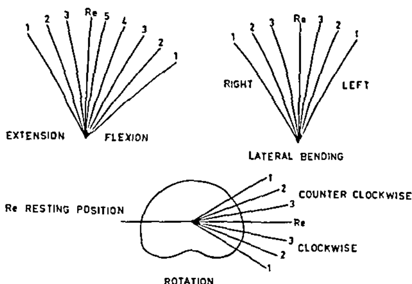


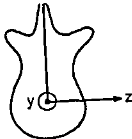
Fig 26 Diagrammatic representation of steps within ranges of motion studied See text for explanation

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From the 17 subjects included in this part of the study the motion of 141 vertebrae was analysed by two programs producing 210 000 informations



5R

5L

5A

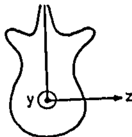
1 g 8 Sh v s t vo v ws of j tt f u ti i Inter l l lig I v r v w l s t l w j o t of sul jac i t rt l r i l tt tl ii ti i b t l i u r f r t u t xt for l scr j tion

x and y axes can again be observed in both the *frontal and horizontal views* This is the same coupling as was seen in lateral bending except that the directions are reversed due to the fact that the specimen was moved from counterclockwise to clockwise the negative direction about the y axis rather than in the positive direction

Flexion and Extension

From the three dimensional analysis information regarding linear movement in the sagittal plane was extracted This was done in order to show for large segments of the thoracic spine what portion of the total sagittal motion could be called extension Thus the linear motion of ball A of the top vertebrae of the thoracic spine segment was divided into two portions These portions were that to the *extension side of the initial resting position (positive direction of x axis) and* that to the flexion side of the initial resting position (negative direction of x axis) The segments of the upper one half of the spine showed a mean percentage extension of 33 4 % of the total range The middle and lower portion showed means of 26 3 and 33 3 % respectively The mean of the percentages of extension for all segments tested was 31 0 % The figures on which these statements are based are given in the Appendix Table VI

The movement to the flexion side and to the extension side of the resting position was compared For each vertebra the movement was separated into what was called the first and second portion of θ range *The first portion was the movement between full extension and the resting position The second portion was the movement between the resting position and full flexion* Only those vertebrae about which there was information on all the steps along the total range were used Inspection of Table VII in the Appendix shows that for a great majority of the vertebrae the amount of extension was less than the amount of flexion For each of the vertebrae Th 1–11 inclusive the means of the movement in the first and then the second portion of range θ were taken In order to look at the over all pattern for the spine the mean total extension for all the vertebrae in all the subjects was compared with the same total for flexion The extension was less than the flexion (1 4 vs 1 9) and was 42° of the full *sagittal motion The full motion in the sagittal plane* was evaluated for this series by taking the total θ_z for each vertebra in the different subject The mean for each level was then calculated and is recorded in Table 6 The angles for individual subjects and vertebrae are given in Table VIII of the Appendix Fig 30 shows the average motion for the different levels of the spine The total of the averages for flexion and extension is 34 4 *The pattern* of cephalocaudal variation shows a tendency for greater sagittal motion at the lower levels



5R

5L

5A

I g 5 Shows tv v ws of patt r of t n lat ral l ing l wer t l n t sl w points of s l jacent vert bra but th r tion t l at l r f r t it s t xt for l cription

Table 6 Means of Total Flexion and Extension for the Various Subjects at Each Level

Vertebral Level	1	2	3	4	5	6	7	8	9	10	11	
Mean θZ	2 8	[illegible]6	2 3	1 8	[illegible]6	3	3 3	3[illegible]	3 1	3 9	6 5	Total 34 4
Range of Mean	2 3	[illegible]7	3 9	2 0	8	2 4	3 1	3 7	[illegible]4	[illegible]7	8 6	

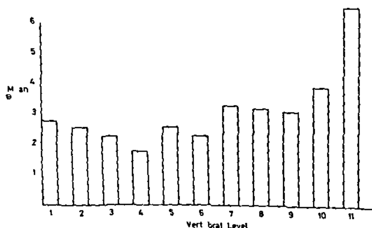


Fig 30 Graph h ws c phalocau lal variat on of flexion exte s on for the sul jects in this series See text for explanat on

Lateral Bending

The motion here is evaluated as described in the preceding paragraph for flexion and extension except that it is rotation about the x axis (θx) that is under consideration The total average movement for all the eleven vertebrae is [illegible]2 0° These observations suggest no particular pattern for cephalocaudal variation See Table 7 and Fig 31 In the Appendix Table IX gives the data for pecific ubjects and vertebrae

T bl 7 M a s f Total Lateral Bend ng for the Var ous Subj cts at Each Level

V rt bral Lev l	1	[illegible]	3	4	5	6		8	9	10	11	
M an θX	6 0	4 5	3	5 0	3	9	4 1	4 7	4 4	4 4	3 7	Total 5 0
Range of M an	6 3	5 6	3 9	[illegible]3	6 3	10 7	5 9	3[illegible]	3 8	4 0	4 4	

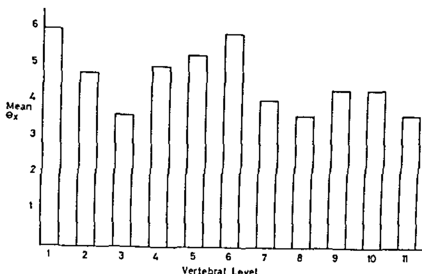


Fig 31 Graph shows cephalocaudal variation of lateral bending for the subjects in this series See text for explanation

Axial Rotation

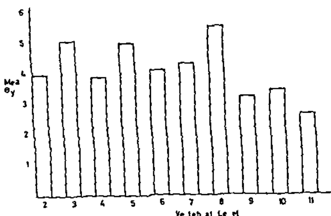
Similar analysis of this movement resulted in the mean angles shown in Table 8 The total of the means for axial rotation is 41 1° Fig 32 suggests less axial rotation at the lower vertebral levels Appendix Table X gives the θy for the various individual subjects and vertebrae The attachment of the rotation apparatus to Th 1 precluded complete observations at that level

Table 8 Means of Total Axial Rotation for the Various Subjects at Each Level

Vertebral Level	1	2	3	4	5	6	7	8	9	10	11	
Mean θy		4 0	5 1	3 9	5 0	4 1	4 3	5 [illegible]	3 [illegible]	3 4	2 6	Total 41 1
Range of mean		3 9	6 4	3 4	[illegible] 4	3 8	4 [illegible]	4 8	3 2	[illegible] 9	[illegible] 5	

Coupling

This aspect of thoracic spine mechanics was evaluated by analysis of the data in the following manner The coupling to be examined is the motion about the x and y axes when the spine moves in lateral bending In other words what is the association if any of θy and θx during lateral bending? In this section the motion discussed is in relation to the external reference point (R) (Fig 24) not to the subjacent vertebra Examination of the data revealed some associated rotation about the z axis during lateral bending Thus it was



F g 3 (raph shows cephalcau lal variat on of ax al rotation for the subjects in this series See text for explanation

necessarv to look at the variation of θ *and* θy when θx was the predominant motion In the lateral movement under analysis that is from complete right lateral bending to complete left lateral bending the major motion is about the x axis to the *positive* direction When there is coupling about the x and y axes a graphic plotting of the cumulative θx and θy of the vertebrae under analysis should show any association that exists In a direct variation coupling the cumulative curve would be positive on both the θy and θx axes An inverse relationship coupling but in the opposite direction would show negative on the θy axis Finally with little or no association (no coupling) the line of cumulative θx and θy values would hunt about the zero point of the θy coordinate As there was some associated θ_z rotation it was necessary to look simultaneously at the cumulative θz and θx *angles* This would make possible a differentiation between specific θx and θy coupling and generalized associated movement including some element of change of θy and θ with θx In this particular coordinate system and for this particular motion a *positive* θy *associated with positive* θx *is the same as rotation of the vertebral body into the concavity of the lateral curve* The 2nd 6th and 11th thoracic vertebrae were selected for analysis of the question of coupling Though it may seem unlikely on initial inspection a study of Figs 33 34 and 35 will elucidate certain information about coupling At the Th2 level four subjects were available for analysis For *all* subjects analysed there was a definite direct relation between

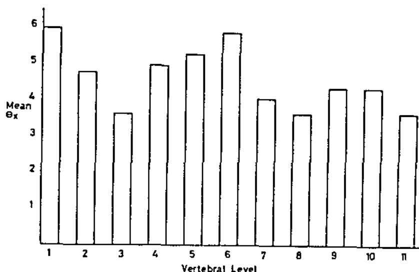


Fig 31 Graph shows cephalocaudal variation of lateral bending for the subjects in this series See text for explanation

Axial Rotation

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Vertebral Level	1	2	3	4	5	6	7	8	9	10	11	
Mean θy		4 0	5 1	3 9	5 0	4 1	4 3°	5 5	3 _	3 4	2 6	Total 41 1
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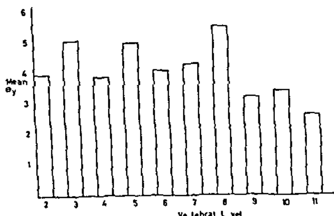


Fig 3 Graph shows cephalocaudal variation of axial rotation for the subjects in this series See text for explanation

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θy and θx At the same time there was very little associated cumulative movement about the θ_z axis This series shows at the Th2 level a definite pattern of coupling of axial rotation into the concavity of the curve with lateral bending (Fig 33)

The motion of Th6 was analysed and depicted in the same manner as Th2 See Fig 34 One can recognize here that there is again a direct variation of θx and θy The relation is not as strong nor as distinctly different from the relation of θx and θ_z as was noted for the Th2 vertebrae There were 11 subjects in which Th6 could be studied The 8 subjects depicted in Fig 34 all showed a relation of positive θy associated with a positive θx In each of the 8 individual cases the positive association of θx and θy was stronger than that of θx and θ for the particular subject under analysis In the remaining 3 cases this situation did not exist Some of the examples at the Th6 level which did not show the pattern of coupling at Th2 actually *showed the reverse* They showed rotation of the vertebrae into the *convexity* of the lateral curve Thus at the Th6 level for this series coupling of axial rotation with lateral bending was found in 8 of 11 examples The rotation in these examples was into the concavity of the lateral curve and not as marked as at the Th2 level

With the same graphing techniques the motion of five Th11 vertebrae was studied Fig 35 shows that some of the subjects demonstrated coupling of motion with positive θx and θy varying directly In these examples 3 out of 5 of the subjects show the coupling of the pattern described above Here too the trend is less strong than at the Th2 level

Average Curvature

So as to have some mathematical description of the steepness of the arch that one vertebra takes in relation to the subjacent one the average curvature was taken Curvature is defined as one divided by the radius (1/r) Thus a very flat arch (that of a huge circle) will have a small value for curvature A steep arch will have a relatively larger value The point used for curvature was the relative motion of point (ball) A between adjacent vertebrae This quantity was calculated for each step in the sagittal and the frontal planes and the average taken for each plane The data is shown for sagittal and frontal motion in Appendix Tables XI and XII respectively The ratio 1/r is multiplied by 100 for convenience Examination of the means of the average curvature for each level in different subjects provides some impression of the over all pattern There is no suggestion of any scheme of cephalocaudal variation in the sagittal plane in the steepness of course traveled by the different vertebrae relative to their subjacent member (Fig 36) In frontal plane motion there is a suggestion of a more steep pattern in the vertebrae at the lower thoracic levels (Fig 37)

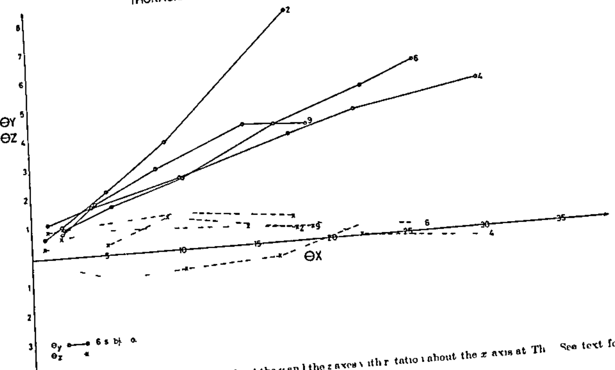


Fig 31 Shows extent of coupling of rotation about the y and the z axes with rotation about the x axis at Th. See text for description.

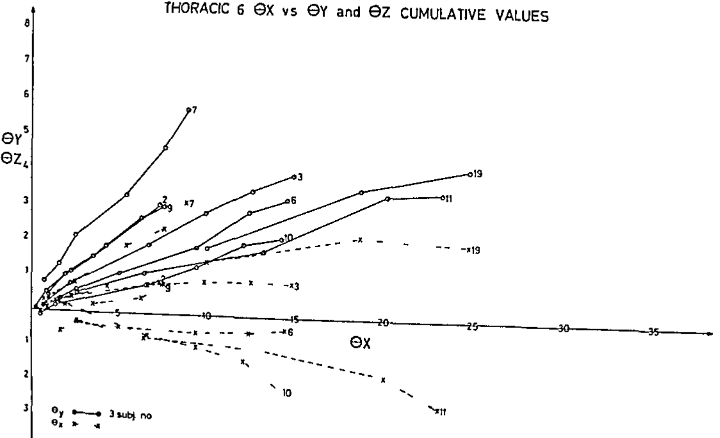


Fig. 31 Shows extent of coupling of rotation about the y and the axes with rotation about the x axis at Th6 See text for description

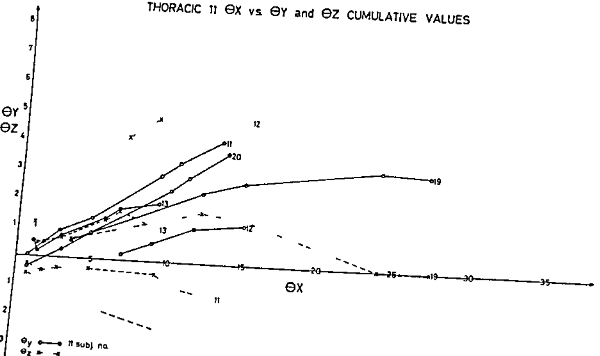
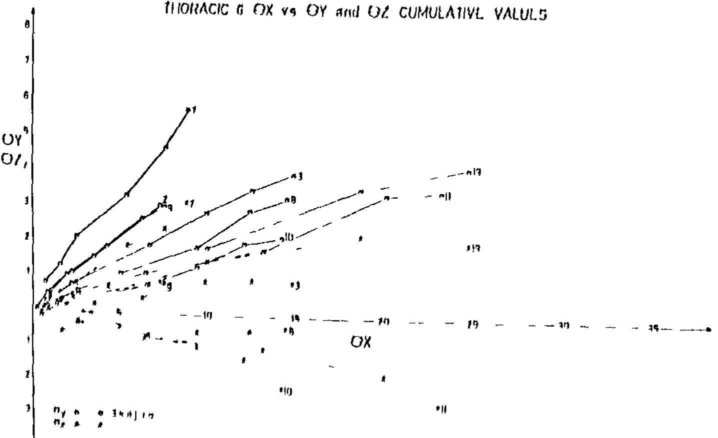
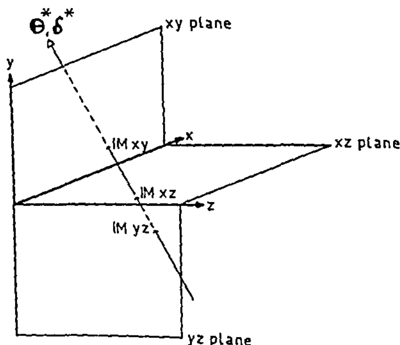


Fig. 35 Shows extent of coupling of rotation about the y and the axes with rotation about the x axis at ThII. See text for description


THORACIC 6 OX vs OY and OZ CUMULATIVE VALUES
OY
OZ
OX
8
7
6
5
3
2
1
1
2
3

The instantaneous motion pattern for a rigid body can be analysed as a simple screw motion The screw motion is a superposition of rotation and translation about and along the same axis (*Christie* 1952 *Shames* 1966) This axis has the same direction as the resultant of the three rotation components about the x y z axes Vector quantities θ^* for rotation and a δ^* for translation lie on this axis The above described axis is referred to as the *helical axis of motion* For a given moving rigid body the location of this axis and the

HELICAL AXIS OF MOTION



$$\Theta^* = \Theta_x^* + \Theta_y^* + \Theta_z^*$$
$$\delta^* = \delta_x^* + \delta_y^* + \delta_z^*$$

Fig. 38 Showing graphical representation of helical axis of motion See text for explanation.

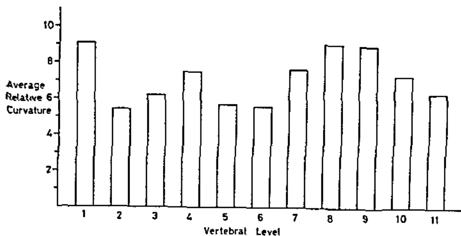


Fig 36 Shows motion curvature in sagittal plane at different vertebral levels See text for explanation

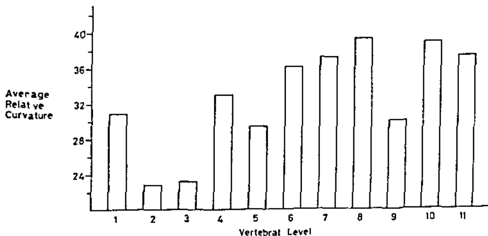
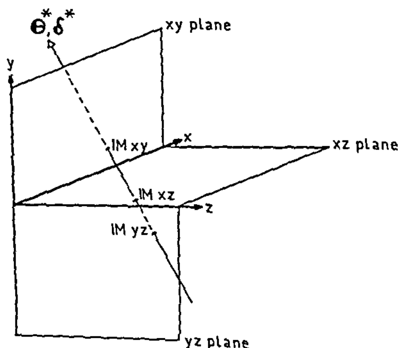


Fig 3 Shows motion curvature in frontal plane at different vertebral levels See text for explanation

Instantaneous Helical Axis of Motion

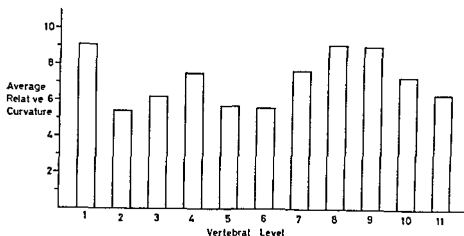
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Fig 38 Shows graphical representation of helical axis of motion See text for explanation



I ig 36 Shows motion curvature in sagittal plane at different vertebral levels See text for explanation

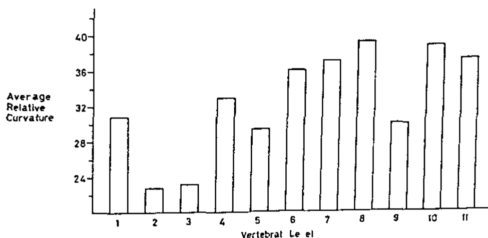


Fig 37 Shows motion curvature in frontal plane at different vertebral levels See text for explanation

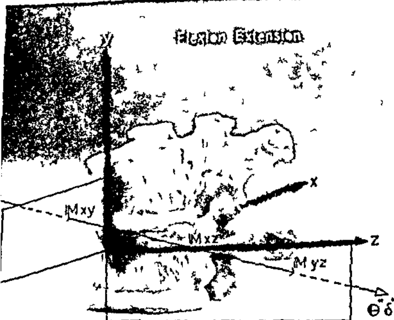
from position 2 to 3 in Fig 26 This motion is in the $-\theta y$ direction The major rotation is negative about the y axis with a very small component of rotation about the z and x axes The translation and rotation of the helical axis is also indicated in this example

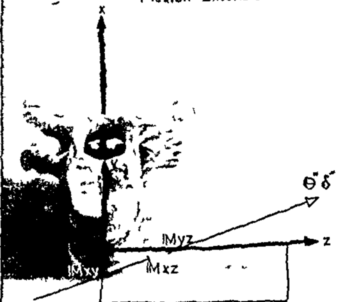
designation of the quantity of its rotation and translation constitute a complete precise three dimensional analysis of the motion In this section a description of the use of this three dimensional analysis on the intersegmental motion of the thoracic vertebrae of man will be presented and exemplified

The reference in relation to which the motion is analysed is point A of the subjacent vertebra The coordinate system is thus established about point A and the respective planes indicated as shown in Fig 38 The position of the resultant axis for any given rotation can be defined by the point at which the axis intersects any two of the three planes Mxy Mxz and Myz Data analysis included calculation of this point of intersection of the helical axis with each of these three planes This calculation was done for every step of flexion extension lateral bending and rotation for all the subjects and all the vertebrae Data processing also included calculation of the ratio of translation to rotation (RTR) along the helical axis

Three examples have been selected quite deliberately to elucidate the characteristic positions of the helical axis of a vertebra in each of the three predominant patterns of motion in the spine The first example Figs 39 and 40 gives the helical axis of motion of Th10 (subject 19) moving in the sagittal plane on the flexion side of the resting position This would be movement from position 5 to 4 on Fig 26 The position of the helical axis in relation to the x y and z axes locates the line about which all points in the vertebra are rotating Also the relative quantities of rotation about the three axes are indicated by the extent to which the helical axis parallels the respective x y and z axes Examination of Fig 39 shows the position of the axis graphically and Fig 40 shows its approximate position in relation to the two vertebrae Additional information in the graphic demonstration is the direction of the helical axis indicated by the arrow which shows that the major rotation is positive about the z axis The lack of parallelism about the y or x axis indicates that there is only a small element of rotation about them The rotation is given by the mathematical analysis and is the vector sum θ^* of the instantaneous rotation about the x y and z axes The translation of the axis is expressed by the vector sum δ^* of the instantaneous translation along the x y and z axes These quantities are indicated in Fig 39 Their symbols are given in Fig 38

Motion in the frontal plane is illustrated by subject 6 Th7 moving from position Re to 3 (Fig 26) The position and direction of the axis indicates predominant rotation about the x axis in the positive direction (Fig 41) There is also a moderate amount of y axis and some z axis rotation involved In this example the helical axis actually goes through the vertebra (Fig 42) The θ^* and δ^* are also shown to complete the analysis by describing the respective rotation and translation of the axis The motion in the horizontal plane is similarly indicated in Figs 43 and 44 The subject is moving in the clockwise direction





10 Shows two vi w of a l cont vert bra th the in tantaneo s helical axis of motion rej resei te l for the *upper* vertebra Motion is from exten on t ar l flexi i S e xt for explai ation

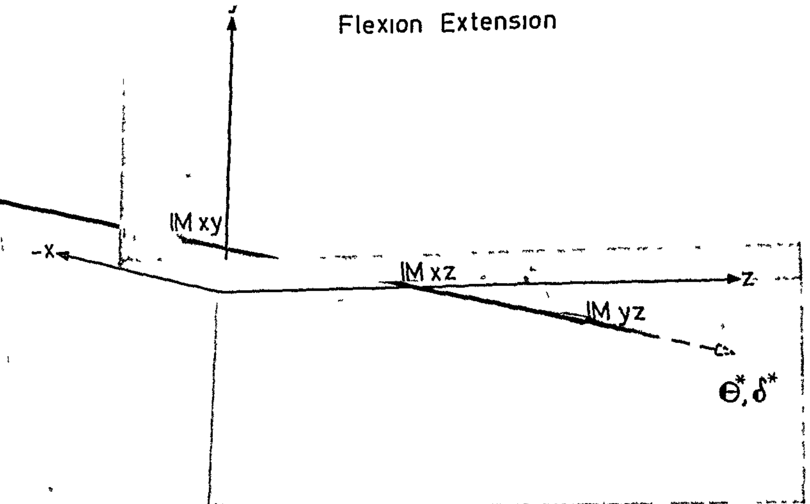


Fig. 39 Plexiglass model constructed to show instantaneous helical axis of motion in three dimensions. Points Mxy, Mxz and Myz were plotted from the actual data on a scale causing a 5:1 magnification.

(— 12 (θ* .)) (— 01 (δ* .))

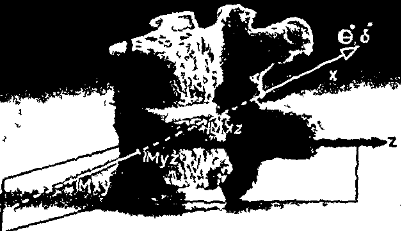


Fig 4 Shows two views of adjacent vertebrae with the instantaneous helical axis of motion represented for the upper vertebra. Motion is from the resting position toward left lateral bending. See text for explanation.

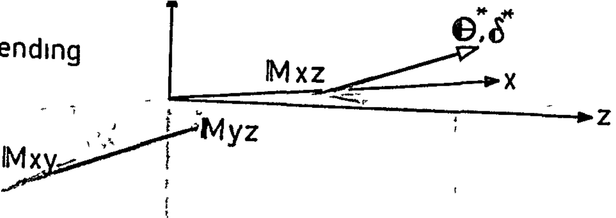
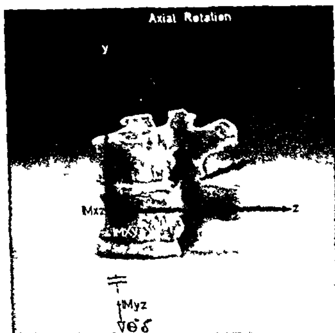


Fig. 41 Plexiglass model constructed to show instantaneous helical axis of motion in three dimensions. Points Mxy, Mxz and Myz were plotted from the actual data on a scale causing a 5:1 magnification

$$\theta^* = \begin{Bmatrix} -99\,(\theta^*_x) \\ 48\,(\theta^*_y) \\ 11\,(\theta^*_z) \end{Bmatrix} \quad \delta^* = \begin{Bmatrix} 27\,(\delta^*_x) \\ 03\,(\delta^*_y) \\ 02\,(\delta^*_z) \end{Bmatrix}$$

RIR 14 14



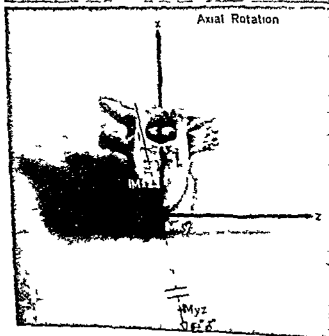


Fig. 44 [illegible] two [illegible] adjacent vertebrae with the [illegible] instantaneous helical axis of motion represented for the upper vertebra. Motion [illegible] from counterclockwise toward clockwise. See text for explanation.

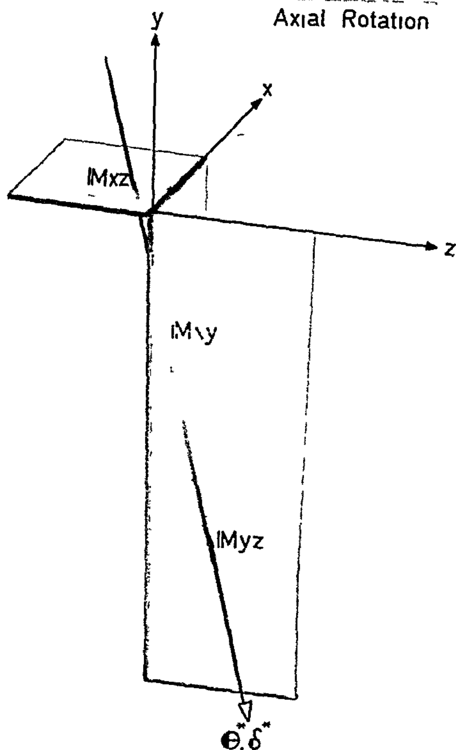


Fig 43 Plexiglass model constructed to show instantaneous helical axis of motion in three dimensions Points M_{xy} M_x and M_y were plotted from the actual data on a scale *causing a 5 1 magnification*

$$\theta^* = \begin{Bmatrix} -.?8 \ (\theta^*\ ) \\ -1.0? \ (\theta^*_y) \\ 3.? \ (\theta^*\ ) \end{Bmatrix} \quad \delta^* = \begin{Bmatrix} -.01 \ (\delta^*\ ) \\ -.0? \ (\delta^*_y) \\ .01 \ (\delta^*_z) \end{Bmatrix}$$

RTR - 68

are precision and thoroughness of description Expression of motion with the helical axis also allows for direct comparison of the motion of bodies of different sizes and shapes Consequently there are no limitations on the choice of the measuring points and secondary measuring points are not required It would not have been possible to introduce the helical axis of motion without the previously mentioned three dimensional mathematical analysis

Comments

The important characteristics of this part of the investigation are the fact that larger segments of the spine were tested and a truly three dimensional analysis of the motion was achieved The method of testing the vertebrae within the full range of their allowable motion afforded observations that may be considered representative of their in vivo behavior The patterns of motion of the individual vertebrae seem to have their own variation of the spinal theme of translation and rotation In the thoracic spine both elements are small Information about the contraversial question of coupling of motion in the thoracic spine is provided by this three dimensional analysis of the data The graphic representation of the sample vertebrae (Th2) showed rotation of the vertebral body into the *concavity* of the lateral curve The graphic analysis of the cumulative angles of rotation showed the same coupling but less markedly and less frequently in the middle and lower portions than in the upper This series supports the conclusion that coupling of the type described is the predominant pattern However this pattern diminishes cephalocaudally It has been shown that there can be essentially no coupling at all or the *reverse* situation of axial rotation into the *convexity* of the lateral curve This was noted at the Th6 level This crucial mechanical point about the behavior of the normal thoracic spine based on three dimensional analysis provides important basic background knowledge relevant to the study of scoliosis In these observations there is again a tendency for the upper part of the thoracic spine to behave somewhat like the cervical spine and the lower part somewhat like the lumbar spine The pattern of coupling noted to be more marked in the upper thoracic spine is characteristic of the coupling of the cervical spine (Lysell 1969) The data from this section of the investigation displayed a propensity for greater flexion extension at the lower portion of the thoracic spine There was also less rotation noted at the caudal end Greater sagittal mobility and less axial rotation are both characteristics of the lumbar spine (*Steindler* 1955 *Gray* 1967 *Gregersen* and *Lucas* 1967)

This part of the investigation is thought to contain the initial introduction of a complete three dimensional analysis of intersegmental spinal motion in terms of the *helical axis of motion* The meaning and interpretation of this type of analysis is described and exemplified The advantages of such a designation

diameter) to the amount of motion did not show any significant correlation Examination of the data for cephalocaudal trends regarding the steepness of arch that each vertebra traveled in relation to its subjacent fellow was made There was no cephalocaudal pattern in sagittal plane motion but a more steep pattern was noted in the caudad half in frontal plane motion

The rather important and contraversial question of coupling was evaluated carefully and the following description is offered In the upper portion of the thoracic spine there is relatively marked and consistant coupling of axial rotation with lateral bending The direction of the coupling is such that the *axial rotation of the vertebral body is into the concavity of the lateral curve* In the middle and also in the lower regions of the thoracic spine this same pattern still exists and probably dominates However it is neither as marked nor as consistantly present Furthermore the direction of the *coupled axial rotation in the middle regions was noted in some cases to be the reverse of the above described pattern* A number of observations were made under controlled conditions on the mechanics of the motion segments with and without their *posterior elements The removal of these structures resulted in significant increases in the amount of motion in flexion in extension and in axial rotation* This information is valuable to the clinician in terms of his understanding of the effects of surgical or traumatic involvement of these structures on the mechanics of the thoracic spine

Analysis of the data to designate the *positions of the instantaneous axes of rotation* in the frontal sagittal and horizontal reontgenographic planes was carried out These points were clustered and fairly consistantly located *for the* ranges tested *For extension they were above the disc for flexion they were below In lateral bending they were at or near the disc and slightly away from the midline to the contralateral side of the direction of lateral bending* The axes in the horizontal plane *with axial rotation tended to cluster at points along a line from the anterior middle portion of the vertebra to the region of the spinal canal* Removal of the posterior elements caused a small but definite shift in the location of these clusters

The portion of this study in which known loads were employed revealed that for the range of loads involved *a spring constant could be determined for the* relationship of force and deformation of the motion segments

From the three dimensional part of this investigation it was possible to introduce the application of the *instantaneous helical axis of motion* in a biomechanical study of the intersegmental motion *of the spine* The designation of the motion in this manner is complete precise graphic and truly three dimensional The instantaneous helical axis of motion was shown for three thoracic vertebrae Each of the three exemplified a different one of the three characteristic movements that is flexion extension lateral bending and axial *rotation*

SUMMARY AND CONCLUSIONS

The clinical importance of the thoracic spine as regards scoliosis, pain syndromes, surgical and traumatic considerations provided the motivation for this investigation. It seemed apparent that reliable descriptive information about the normal mechanical function of this region of the spine would serve as a basis for better understanding of disease and therapy. Inquiry of the available literature on the motion of the thoracic spine pointed up the fundamental questions to be answered in a thorough description. Previous studies have not combined precise modern techniques with substantial numbers of subjects and reported on all parameters of the motion. Consequently there is considerable variation among statements in the literature about the motion of the thoracic spine.

There are available at present two well developed and accurate biomechanical experimental methods to describe movement of rigid bodies. One method has been used effectively in the lumbar spine, the other in the cervical spine. The information offered by the two methods is similar, different and complementary. Thus it was elected to employ them both in this investigation.

In view of the fact that the goal of this endeavour was to offer descriptive information about the mechanics of the thoracic spine, this summary of the results will begin with general descriptive remarks based on measurements and analysis of the data from both parts of the investigation. There is wide variation among the different subjects and different vertebrae of the same subject both in terms of quantity and quality of motion. Nevertheless some general patterns emerge. There is *more flexion than extension*. One can expect *2–6° of motion at each interspace in the sagittal plane, 30–42%, of which will be extension, the rest flexion. At the lower thoracic levels, especially* Th10 *and* Th11 *there is relatively more sagittal plane motion. Lateral bending is in the range of 3–6° at each interspace.* No pattern of cephalocaudal variation emerged here. The total motion in this plane was found to be greater than for the sagittal plane. *Axial rotation was in the range of 2–6° with the most caudal portion* (Th10 *and* Th11) *at the lower end of that range.*

Other findings related to specific questions are also summerized here. This data did not show any correlation positive or negative between age and amount of motion. Tests of the relationship of the motion ratio (disc height/disc

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This descriptive analysis of the normal thoracic spine includes some considerations of considerable clinical import especially in the field of traumatology The characteristic patterns and ranges of motion for the different portions of the thoracic spine is of value in the interpretation of and the protection from offending forces The same information assists in the recognition of those portions most likely to be susceptible to damage by forces of particular magnitudes and directions Even more important perhaps is the complete mathematical description of three dimensional motion employing the helical axis of motion The use of this thorough precise mathematical description in conjunction with the spring constant offers extensive possibilities Examples would be the construction of representative mechanical models and the accurate mathematical prediction of expected behavior of the spine in response to normal and pathological forces

The findings of this investigation of 27 autopsy specimens admit the following remarks about the thoracic spine Its upper and lower portions behave quite differently and have certain traits suggestive of their neighboring adjacent regions of the spine That portion of the spine between the two extremes is fairly homogenous in most of its characteristics none of which are particularly distinguishing The main generalization that characterizes this region of the spine situated in the thorax is that it moves very little

The analysis of the mechanics has been carried out and presented in a manner that can be meaningfully interpreted and employed by the biological as well as the engineering scientist

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APPENDIX

Table [illegible]. Sums of Ranks for Statistical Interpretation of Cephalocaudal Variations of [illegible] for all Subjects*

Level [illegible]	Th 1–[illegible]	Th 3–4	Th 5–6	Th [illegible]–8	Th 9–10	Th 11–[illegible]
Sums [illegible] Ranks						
[illegible]						
[illegible]	[illegible]	4	5	3	12	17
[illegible]	4	9	[illegible]	3	[illegible]	15
[illegible]						
[illegible]	14	3	8	[illegible]	11	17
[illegible]	3	4	3	9	11	14
[illegible]						
[illegible]	12	12	6	[illegible]	9	[illegible]
[illegible]	[illegible]	11	3	3	11	12
[illegible]						
[illegible]	14	1	8	4	9	[illegible]
[illegible]		10	4	10	10	11
[illegible]	14	[illegible]	10	1	9	[illegible]
[illegible]	11	12	10	10	4	6

* Reading from [illegible] any difference among the [illegible] of six numbers equal to [illegible] can be [illegible] significant at the .10 level of confidence. Thus, the [illegible] movements [illegible] different vertebral levels may be compared.

† [illegible] used [illegible] "Balanced incomplete block design" [illegible] D. R. Planning of experiments. Wiley, New York, [illegible]

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APPENDIX

Table I Sums of Ranks for Statistical Interpretation of Cephalocaudal Variations of Slopes for all Subjects

Level of MS	Th 1-2	Th 3-4	Th 5-6	Th 7-8	Th 9-10	Th 11-12
Sums of Ranks						
Sag ttal Intact						
pos t on	1[illegible]	8	5	9	13	13
75° pos t on	8	9	7	9	1[illegible]	15
Sagitt l W tho t PE						
[illegible] pos t on	14	9	6	7	11	13
75 pos t on	9	8	9	9	11	14
Frontal Inta t						
5 p ition	13	13	6	7	9	1[illegible]
5 position	[illegible]	11	9	9	11	13
Frontal W thout PE						
5 po it on	14	11	6	8	9	1[illegible]
75 position	11	10	8	10	10	11
R tat n Inta t	14	11	10	11	9	5
R tation W thout PE	11	15	10	10	8	6

Reading from l ft to right any difference among the groups of six numbers equal to or greater than 7 can be con idered significant at the 0 10 le el of confidence Thus the sl pes for th indicated mo ements at d fferent vertebral l vels may be compared

St t st s based on Balanced ncomplete block des gn Cox D R Planning of ex pe iments Wiley N w York 19 [illegible]

Table II Standardized Motion of the Various Subjects and Vertebral Levels Under Different Loading Conditions*

Vertebral Level		Th 1–2 25%	Th 1–2 75%	Th 1–2 Combined	Th 3–4 25%	Th 3–4 75%	Th 3–4 Combined	Th 5–6 25%	Th 5–6 75%	Th 5–6 Combined	Th 7–8 25%	Th 7–8 75%	Th 7–8 Combined	Th 9–10 25%	Th 9–10 75%	Th 9–10 Combined	Th 11–12 25%	Th 11–12 75%	Th 11–12 Combined
Subjects																			
IV	SI	1.10	0.70	1.80	0.80	0.70	1.00	1.30	1.00	2.30	4.90	3.70	8.60	1.90	0.55	2.45	3.85	2.20	6.05
	SS	2.60	3.20	5.80	2.80	2.30	5.10	2.05	2.00	4.05	4.90	6.35	11.25	2.20	3.20	5.40	8.25	8.60	16.85
	FI	0.20	1.15	1.35	1.20	2.25	3.45	0.95	0.65	1.60	2.30	3.05	5.35	1.05	0.95	2.00	3.25	3.80	7.05
	FS	2.45	4.00	6.45	1.55	2.55	4.10	1.30	0.50	1.80	3.10	3.15	6.25	0.95	1.40	2.35	3.70	4.35	8.05
	RI	9.60			1.95			8.65			14.05			1.70			0.90		
	RS	16.70			5.05			13.85			18.55			1.95			2.35		
V	SI				1.55	0.70	2.25				5.75	7.70	13.45	10.20	4.75	14.95	27.80	17.70	45.50
	SS				5.25	5.55	10.80				7.70	14.70	22.40	9.80	13.10	22.90	23.50	18.10	41.60
	FI				2.75	1.70	4.45				6.60	6.00	12.60	7.80	2.80	10.60	15.00	10.30	25.30
	FS				3.25	2.00	5.25				12.00	11.40	23.40	10.50	1.20	11.70	17.60	11.20	28.80
	RI				12.80						13.05			5.95			4.35		
	RS				19.90						13.50			8.15			9.45		
VI	SI				6.55	3.45	10.00	2.40	2.90	5.30	8.50	1.10	9.60	6.50	0.40	6.90	14.30	9.90	24.20
	SS				11.35	7.85	19.20	3.40	8.30	11.70	3.70	4.35	8.05	3.45	4.60	8.05	14.30	18.20	32.50
	FI				5.20	3.10	8.30	3.95	4.00	7.95	2.70	2.00	4.[illegible]0	2.40	3.35	5.75	5.10	3.70	8.80
	FS				5.20	6.90	12.10	5.80	5.00	10.80	3.05	1.75	4.80	1.15	1.15	2.60	5.60	7.10	12.70
	RI				15.30			12.00			12.65						11.20		
	RS				21.20			19.00			16.25						11.80		
VII	SI	5.30		5.30	2.80	0.25	3.05	7.10	1.65	8.75	6.35	2.20	8.55	11.85	3.50	15.35			
	SS	8.20	1.35	9.55	3.40	3.60	7.00	5.70	5.70	11.40	5.60	4.10	9.70	10.60	7.10	17.70			
	FI	13.40	2.95	16.35	4.60	3.00	7.60	6.90	1.15	8.05	8.45	5.[illegible]0	13.65	6.70	3.85	10.55			
	FS	13.40	3.10	16.[illegible]0	3.10	3.25	6.35	5.10	1.90	7.00	7.05	4.30	11.35	4.85	3.85	8.70			
	RI	19.20			10.05			18.00			11.20			5.70					
	RS	28.10			20.80			25.05			18.20			6.35					

SI Sagittal intact
SS Sagittal without posterior elements
FI Frontal intact
FS Frontal without posterior elements
RI Rotation intact
RS Rotation without posterior elements
* Missing entities due to a variety of experimental conditions

Table II *Continued*

Vertebral Level		Th 1-2			Th 3-4			Th 5-6			Th 7-8			Th 9-10			Th 11-12		
		5	5	Combined	5	75	Combined		5	Combined	5	75	Combined	5	75	Combined		75	Combined
Subjects																			
VIII	SI	4 85	0 0	5 05				4 80	0 80	5 00	5 0	_40	7 60						
	SS	*6 10*	*1 80*	*8 0*				4 0	3 90	8 50	3 80	11 30	15 10						
	FI	5 00	0 85	5 85				95	00	55	5 60	3 30	8 90						
	FS	4 0	1 0	6 40				_60	4 75	6 95	5 70	6 30	12 00						
	RI	1 50						15 0			15 30								
	RS	7 90						18 50			0								
IX	SI	6 05	0 60	6 65	0	1 10	3 30	10	0 40	50	3 0	0 70	3 90	4 0	1 0	5 40			
	SS	7 0	4 0	11 40	3 40	70	6 10	*0 50*	*0 0*	*0 70*	*3 5*	10	*5 35*	4 65	3 10	5			
	FI	1 95	3 5	*5 0*	95	60	5 55	40	1 40	3 80	1 40	1 70	3 10	30	1 70	4 00			
	FS	5 40	5 00	10 40	80	1 85	4 65	0 90	0 40	1 30	1 50	3 30	4 80	1 85	3 0	5 05			
	RI	4 40			1 10			8 10			0 0			4 50					
	RS	16 60			16 10			11 0			11 30			0 0					
X	SI	5 0	1 75	7 55	4 75	1 30	6 05	0 75	0 50	1 5	0	05	4 5	3 35	_ 0	6 05	55	1 70	4 5
	SS	8 0	0 50	0 0	6 0	85	9 05	1 15	1 40	_55	3 0	3 00	6 0	5 65	4 35	10 00	3 75	80	6 55
	FI	90	1 40	4 30	6 0	6 95	13 15	1 80	30	4 10	4 05	40	6 45	5 75	3 90	9 65	30	2 40	4 70
	FS	5 0	_60	8 30	6 00	5 80	11 80	1	1 75	3 90	10	3	8 3	5 35	3 85	9 0	3 45	0	7 95
	RI	16 30			14 75			4 00			4 10			3 15			1 05		
	RS	5 00			19 10			*5 70*			4 0			3 55			0 90		

SI *Sagittal intact*
SS Sagittal without posterior elements
FI Frontal intact
FS Frontal without posterior elements
RI Rotation intact
RS Rotation without posterior elements

Table II Standardized Motion of the Various Subjects and Vertebral Level Under Different Loading Conditions*

Vertebral Level		Th 1–2 25%	Th 1–2 75%	Th 1–2 Combined	Th 3–4 25%	Th 3–4 75%	Th 3–4 Combined	Th 5–6 25%	Th 5–6 75%	Th 5–6 Combined	Th 7–8 25%	Th 7–8 75%	Th 7–8 Combined	Th 9–10 25%	Th 9–10 75%	Th 9–10 Combined	Th 11–12 25%	Th 11–12 75%	Th 11–12 Combined
Subjects																			
IV	SI	1.10	0.70	1.80	0.80	0.20	1.00	1.30	1.00	2.30	4.90	3.70	8.60	1.90	0.55	2.45	3.85	2.20	6.05
	SS	2.60	3.20	5.80	2.80	2.30	5.10	2.05	2.00	4.05	4.90	6.35	11.25	2.20	3.20	5.40	8.25	8.60	16.85
	FI	0.20	1.15	1.35	1.20	2.25	3.45	0.95	0.65	1.60	2.30	3.05	5.35	1.05	0.95	2.00	3.25	3.80	7.05
	FS	2.45	4.00	6.45	1.55	2.55	4.10	1.30	0.50	1.80	3.10	3.15	6.25	0.95	1.40	2.35	3.70	4.35	8.05
	RI	9.50			1.95			8.65			14.05			1.70			0.90		
	RS	16.70			5.05			13.85			18.55			1.95			2.35		
V	SI				1.55	0.70	2.25				5.75	7.70	13.45	10.20	4.75	14.95	27.80	17.70	45.50
	SS				5.25	5.55	10.80				7.70	14.70	22.40	9.80	13.10	22.90	23.50	18.10	41.60
	FI				2.75	1.70	4.45				6.60	6.00	12.60	7.80	2.80	10.60	15.00	10.30	25.30
	FS				3.25	2.00	5.25				12.00	11.40	23.40	10.50	1.20	11.70	17.60	11.20	28.80
	RI				12.80						13.05			5.95			4.35		
	RS				19.90						13.50			8.15			9.45		
VI	SI				6.55	3.45	10.00	2.40	2.90	5.30	8.50	1.10	9.60	6.50	0.40	6.90	14.30	9.90	24.20
	SS				11.35	7.85	19.20	3.40	8.30	11.70	3.70	4.35	8.05	3.45	4.60	8.05	14.30	18.20	32.50
	FI				5.20	3.10	8.30	3.95	4.00	7.95	2.20	2.00	4.20	2.40	3.35	5.75	5.10	3.70	8.80
	FS				5.20	6.90	12.10	5.80	5.00	10.80	3.05	1.75	4.80	1.15	1.45	2.60	5.60	7.10	12.70
	RI				15.30			12.00			12.65						11.20		
	RS				21.20			19.00			16.25						11.80		
VII	SI	5.30		5.30	2.80	0.25	3.05	7.10	1.65	8.75	6.35	2.20	8.55	11.85	3.50	15.35			
	SS	8.20	1.35	9.55	3.40	3.60	7.00	5.70	5.70	11.40	5.60	4.10	9.70	10.60	7.10	17.70			
	FI	13.40	2.95	16.35	4.60	3.00	7.60	6.90	1.15	8.05	8.45	5.20	13.65	6.70	3.85	10.55			
	FS	13.40	3.10	16.50	3.10	3.25	6.35	5.10	1.90	7.00	7.05	4.30	11.35	4.85	3.85	8.70			
	RI	19.20			10.95			18.00			11.20			5.70					
	RS	28.10			20.80			25.05			18 0			6.35					

SI Sagittal intact
SS Sagittal without posterior elements
FI Frontal intact
FS Frontal without posterior elements
RI Rotation intact
RS Rotation without posterior elements
* Missing entities due to a variety of experimental conditions

Tal l III Mc ns f Stan lar lized Motion of all Sul j t U i ler Va ou s I oa l ng Co i l t on at tl Vario is Vertel ral Levels

V t l ral Lev l	Th 1			Th 3 4			Th 5 6			Th 7 8			Th 9 10			Th 11-1		
	5	75	Com l i l	5	5	Com l i l	5	5	Com l ne l	25 o	5	Com l ne l	5	75	Com l ne l	5	7	Com l ne l
MSI	4 34	0 C)	4)	3 45	1 1	4 91	3 1	1 09	4 30	5 ,7	63	8 0	5 86	6	9 1	[illegible]	7 11	10 43
MSS	6 68	1	8 89	4 84	4 3	9 33	3 0	3 31	6 45	4 46	5 84	10 30	5 75	5 43	11 18	11 39	[illegible]	23 68
MFI	4 69	[illegible]	0 61	3 08	3 1	7 19	3 4	2 10	5 40	3 87	3 34	7 1	3 83	3 04	6 87	7 19	6 15	13 34
MFS	6 33	3 8	0 61	3 49	3 89	7 39	8		5 04	4 33	4 41	8 74	3 67	6	6 9	9 71	6 91	1o 61
MRI	13 06			10 08			10 49			10 36			4 57			3 30		
MRS	C6			10 44			13 8			13 47			5 31			4 66		

MSI Mea i sagittal intact
MSS Mean g ttal i thou t p o te or le nents
MFI Mean frontal nta t
MFS M an front l i ithout post r or elem nts
MRI Mea i r tat on intact
MRS M an rotat on witho it po terior ele nents

Table II *Continued*

Vertebral Level		Th 1–2			Th 3–4			Th 5–6			Th 7–8			Th 9–10			Th 11–12		
		25%	75%	Combined	25%	75%	Combined	25%	75%	Combined	25%	75%	Combined	25%	75%	Combined	25%	75%	Combined
Subjects																			
XI	SI				6 65	1 10	7 75	5 50	1 00	6 50	8 85	2 30	11 15	7 85	2 80	10 65		6 50	
	SS				5 10	3 80	8 90	4 65	3 65	8 30	4 50	5 15	9 65	8 70	6 15	14 85		13 80	
	FI				6 05	1 95	8 00	3 50	2 00	5 50	2 05	2 50	4 55	4 80	4 90	9 70	8 30	7 40	15 70
	FS				3 85	4 05	7 90	2 15	1 70	3 85	0 80	3 35	4 15	5 25	4 20	9 45	6 90	8 60	15 50
	RI				11 25			12 70			11 05			6 40			0 60		
	RS				17 80			11 10			13 00			6 70			1 20		
XII	SI				4 25	1 60	5 85	3 10	0 90	4 00	8 80	0 95	9 75	4 50	1 95	6 45	18 90	7 05	25 95
	SS				3 20	5 20	8 40	3 00	1 40	4 40	6 05	3 00	9 05	4 30	4 30	8 60	12 75	19 10	31 85
	FI				5 60	4 60	10 20	5 15	2 25	7 40	3 20	1 95	5 15	0 70	2 40	3 10	12 90	10 95	23 85
	FS				4 65	5 95	10 60	3 65	2 30	5 95	1 90	3 30	5 20	0 65	2 80	3 45	20 35	10 70	31 05
	RI				12 60			8 90			5 70			4 95			4 45		
	RS				15 15			12 35			8 35			5 35			4 90		
XIII	SI	2 95	0 20	3 15	1 50			1 80	0 70	2 50	1 90	3 15	5 05	2 40	2 50	4 90	5 90	4 70	10 60
	SS				2 90			2 00			1 90	4 35	6 25	2 40	3 00	5 40	5 70	7 05	12 75
	FI				1 30	2 70	4 00	1 55	3 10	4 65	2 80	5 25	8 05	3 00	3 50	6 50	3 50	4 50	8 00
	FS				1 05	2 70	3 75	1 70	2 20	3 90	3 10	4 00	7 10	2 50	1 65	4 15	3 35	3 90	7 25
	RI	12 85			7 10			6 40			7 30			4 20			0 95		
	RS	21 65			12 90			7 80			8 80			3 90			2 00		

SI Sagittal intact
SS Sagittal without posterior elements
FI Frontal intact
FS Frontal without posterior elements
RI Rotation intact
RS Rotation without posterior elements

Table V Rank Order of Disc Height/Disc Diameter With Associated Total Sagittal Motion of Th 7–8 for Each Subject

Motion Ratio × 100 Disc Height/Disc Diameter	Subject	Sagittal Intact	Sagittal Without Posterior Elements
8 90	VI	9 6	8 1
9 90	IV	8 6	11 3
9 90	XII	9 8	[illegible] 1
9 9	X	4 3	6
1 35	XI	11 [illegible]	9 7
1 6	IX	4 0	5 4
1 98	XIII	5 1	6 3
16 35	VIII	7 6	15 1
17 19	V	13 5	4
18 18	VII	8 6	9 [illegible]
	Coefficient of correlation	0 05	0 [illegible]5

Table V (cont.) Rank Order of Disc Height/Disc Diameter With Associated Total Frontal Motion of Th 7–8 for Each Subject

Motion Ratio × 100 Disc Height/Disc Diameter	Subject	Frontal Intact	Frontal Without Posterior Elements
8 3	IV	5 4	6 3
9 46	XI	4 6	4 [illegible]
10 34	IX	3 1	4 8
11 60	VII	13 7	11 4
1 50	XIII	8 [illegible]	7 1
1 85	VI	4 [illegible]	4 8
1 90	XII		5 [illegible]
13 6	X	6 5	8 4
14 06	V	1[illegible] 6	[illegible]3 4
15 00	VIII	8 9	1 0
	Coefficient of correlation	0 17	0 7

Table IV Sums of Ranks for Statistical Interpretation of Cephalocaudal Variation of the Mean Values for Extracted Angles at 6 Kp/cm Load and 20 Kp cm Moment For all Subjects*

Level of MS	Th 1–2	Th 3–4	Th 5–6	Th 7–8	Th 9–10	Th 11–12
Sums of Ranks at 6 kp/cm load						
Sagittal Intact						
25% position	10	7	5	11	13	14
75% position	8	9	7	10	12	14
combined	10	8	6	11	11	14
Sagittal Without PE						
25% position	13	9	6	7	11	14
75% position	8	7	9	10	11	15
combined	10.5	8	6.5	10	11	14
Frontal Intact						
25% position	10	12	7	8	9	14
75% position	8	8	9	12	9	14
combined	10	11	7	11	7	14
Frontal Without PE						
25% position	12	9	8	10	7	14
75% position	10	8	7	13	10	12
combined	12	8	8	10	8	14
Sums of Ranks at 20 kp cm moment						
Rotation Intact	13	12	11	11	8	5
Rotation Without PE	15	13	10	10	7	5

* Reading from left to right any difference among the groups of six numbers equal to or greater than 7 can be considered significant at the 0.10 level of confidence. Thus the extracted angles of motion at different vertebral levels may be compared.

Statistics based on Balanced incomplete block design. Cox D R Planning of experiments Wiley New York 1958

T bl VII Sh A gl f Motio n Flex on and E t o f r I d t l V rt b a of the D ff rent S bjects

I xten

S bj t	1		3	4	5	6	7	8	9	10	11	1	13	14	15	19	0	Means
V rt bral Le l																		
1			35	1 81		0 55	1 00											1 5
		0 83	1 73	1 7.	1 10	0 44	14										0 40	1 1
3			1 00	1 .8	0 56	0 17	0 9	1 43	0 9					0 39	0 12			0 9
4		0 35	0 87	0 98	0 69	1 04	0 7	0 94	0 80					1 36	0 17		0 45	0 8
5			0 80	1 66	0 70	0 9.	1 11	1 87	0 66	0 53				1 07	0 85	1 13	4.	1 -
0	0 10		1 56	1 39	1 64	0 0	0		0 55	0 6	0 ?		-0 07		1 1-	1 31	0 67	0 8
	0 4	0 99	1 6	3			1 5	1 77			0 0?		0 78	1 30	? 33	? 17		1 4
8	0 1									0 13	0 56		1 14	1 90	? 94	1 5		1 3
9	0 5									0 60	0 57	1 19	1 13		- 35	1	1 6	1 3
10	0 6									1 08	0 67	0 95	1 c3		3 16	61	1 90	1 6
11											0 83	1 8.	1 6			31	10 48	3 5

Av rage of Means 1 4

Fl xion

Subj t	1		3	4	5	6	7	8	9	10	11	1	13	14	15	19	0	Means
V t bral Le l																		
1			1 16	1 44		1 15	1 91											1 4
		1 75	1 c3	1 98	0	1 .9	1 69										1 76	1 5
3			1 03	1 0	0 58	1 6	0 53	1 17	0 84					0 50	0 4.			1 0
4		0 43	0 96	1 40	0 40	1 61	1 03	0 96	0 .3					0 67	0 41		3 09	1 0
5			1 5	1 30	1 13	98	0 94	0 6?	0 90	0 4				?9	1 08	1 49	- 16	1 4
6	0 6.		1 03	1 96	1 1.	2 16	1 ?9		0 8.	-0 1.	0 19		1 84		2 3	- .9	3 6(	1 5
7	0 68	1 49	- 19	01			19	3 6			0 .6		1 53	57	3 .4	- 4		2 0
8	1 00									1 17	1 03		2 48	?78	3 57	2 7		? ?
9	1 53									1 17	1 34	1 87	10		?76	2 38	? 93	? 0
10	1 80									1 13	1 47	1 17	11		6 1?	- 71	3 95	- 6
11											-06	84	3 03			4 33	3 84	3 4

Average of M ans 1 9

Table VI Shows Amount of Linear Movement in Sagittal Plane and Percentage of Extension

Portion of Thoracic Spine	Extension (mm displacement on X axis to resting position)	Flexion (mm displacement on X axis beyond resting position)	Total	% Extension
1–7	12 20	24 60	36 80	33
1–7	19 60	33 38	52 98	37
1–7	12 73	19 98	32 21	39
1–7	11 42	27 61	39 03	29
1–7	12 78	27 27	40 05	32
1 7	10 15	35 78	45 93	22
1–6	10 58	17 18	27 76	38
1–8	25 20	48 30	73 50	34
2–7	6 38	11 87	18 25	35
			Mean	33 4
			Range of Mean	30 5
6–11	7 20	29 40	36 60	29
6–11	19 87	32 79	52 66	33
6–10	6 30	17 26	23 56	17
			Mean	20 3
			Range of Mean	23 0
4–11	24 40	54 95	84 35	34
3–10	40 85	74 72	115 57	35
5–10	10 30	21 90	32 20	31
			Mean	33 3
			Range of Mean	32 5

Mean of % Extension for all Segments 31 0%
Range of Mean 28 0

Table IX Lateral Bending Total θ_x

Subjects	1		3	4	5	6	7	8	9	10	11	1?	13	14	15	19	0
Vertebral Level																	
1			46	5 5		10 05											
2		1 ?	10 0	98		6 8			3 63								
3		3 99	0 63	5 17		1 07	1 8		3 70								
4		1 85				0 19	59		1 04								13 70
5		3 79	0 13	0 5?		1 70	3 41		8?				10 9?		8 15		4 4
6		? 9	4 47	0 46		5 4	1 3		1 9	64	3 43		66		1 13	0 97	3 40
7	4 48	1 14	4 70	0 53			1 34			?	07				10 47	4 18	/
8	5 69									0 78	4 59				1 0	3 40	
9	1 74												r 6		4 58		5 80
10	1 53												39		0 04	6 50	43
11											34					7 78	1 03

Table VIII Flexion Extension Total θz

Subjects	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	19	20
Vertebral Level																	
1			3 51	3 25		1 70	2 90										
2		2 58	3 42	3 65	1 82	1 72	2 82										2 16
3			2 12	2 00	1 14	1 79	1 32	2 60	1 63					1 18	6 61		
4		0 78	1 83	2 38	1 09	2 65	1 75	1 90	1 33					2 03	0 58		3 54
5			2 50	2 96	1 83	3 97	2 05	2 49	1 46	0 95				3 35	1 93	2 62	4 61
6	0 88		2 59	3 25	2 76	2 86	1 91		1 37	0 41	0 41		1 84		3 35	3 60	4 33
7	1 10	2 48	3 45	4 54			3 44	5 39			0 58		1 53	3 87	5 57	4 41	
8	1 27									1 80	1 59		2 48	4 66	6 06	4 24	
9	2 05									1 77	1 91	3 06	2 10		5 11	4 50	4 55
10	2 42									2 21	2 14	2 12	2 11		9 37	5 32	5 85
11											2 89	4 69	3 09			7 24	14 32

Table IX Lateral Bending Total θx

Subjects	1		3	4	5	6	7	8	9	10	11	1	13	14	15	19	0
Vertebral Level																	
1			46	5 5		10 05											
		1	10 0	98		6 28			3 83								
3		3 98	0 63	5 17		1 07	1 8		3 16								
4		1 85				0 18	2 59		1 04								13 0
5		3 78	6 13	6 5		1 0	3 41		8				10 92		8 15		4 4
6		8	4 47	0 40		5 4	1 3		1 8	84	3 43		2 66		1 03	0 97	3 49
7	4 45	1 34	4 0	0 53			1 34				07				10 47	4 18	/
8	5 09									0 8	4 78				4 02	3 46	
9	1 74												5 96		4 58		7 86
10	1 53												2 38		6 04	6 0	5 43
11											2 34					7 78	1 03

Table X Axial Rotation Total θ_y

Subjects	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	19	20
Vertebral Level																	
1																	
2		2 09	6 73	4 87		5 15	4 71		3 64					1 06			
3		0 91	5 87	3 92		11 95	3 36		2 94					6 25			6 56
4		1 69	5 29	3 06			3 65		3 99					5 20		3 64	4 45
5		2 95	4 83	2 64		7 92	3 64		3 07	3 60			5 86		8 13		6 97
6	2 65	3 22	3 85	3 49		1 32	3 99		1 73	3 84	5 69		5 43		5 01		5 76
7	1 68	2 78	3 7							3 82	6 35	3 94	5 21	5 30	6 67		
8	2 29										6 89		4 46		7 32	6 53	
9	1 45									3 78			3 64		3 96	5 0	0 99
10	0 50									2 12		5 41	2 40		3 58	4 64	5 03
11												- 77				2 70	2 19

Table XI Average Relative Curvature Sagittal 1/r ×100

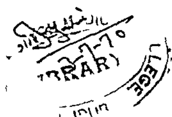
Vertebral Level	1	2	3	4	5	6	7	8	9	10	11
Subjects											
1						3 70	6 41	6 07	2 38	5 09	
2		3 98		6 38			6 41				
3											
4	6 6	5 16	6 13	4 47	3 79	5 14	40				
5		5 01	4 50	11 33	12 66	4 64					
6	8 69	5 25	4 85	4 58	5 03	5 0					
7	11 98	5 38	3 74	4 47	5 18	7 35	7 49				
8			8 00	5 6	4 34		6 56				
9			4 41	4 63	4 96	3 48					
10					4 66			5 01	6 15	2 84	
11						4 04	7 56	10 88	6 64	12 75	0
1											
13						7 39	10 78	4 3	6 95	6 81	9 6
14			14 39	6 86			5 14	6 63			
15			3 99	1 97	4 4	11 99	7 84	85	30 38	10 79	
19					11 90	4 60	11 94	3 44	5	6 48	5 95
0		7 8		14 7	1 96	5 00			96	7 48	5 11
Means	9 07	5 43	6 5	7 57	5 8	5 68	7 5	9 17	9 10	39	6 44
Range of Mean	9 7	5 90	9 07	9 37	7 59	7 4	8 49	13 88	16 38	8 00	7 34

Table XII Average Relative Curvature Frontal 1/r ×100

Vertebral Level	1	2	3	4	5	6	7	8	9	10	11
Subjects											
1						1 43	36 79	34 44	14 3	96	
		4 43		39 11	5 93		40 0				
3	4 0	3 8	3 00		3 95	4 0	6 31				
4	38 0	9 80	3 79		37	9 55	3 04				
5											
6	49 8	30 49	8 1	6 8	9 50	31 1	36 07				
			1 97	6	30 3	4 01	43 45				
8											
9		5 9	6 9	9	6 1	07					
10						47 3	49				
11					6 34	3 06	43 0				
1											9 36
13											
14									39 35	38 97	55 57
15					36	67 5	44 8	44 69		9 53	
19					66 87	7 46	68 1		9 97	3 1	34 80
0				44 96		8 7			3 09	4 69	30 47
Mean	30 84	88	3 19	33 0	8 5	36 3	3 33	39 57	30 16	41 6	3 55
Range of Means	4	17 13	0 0	33 60	3 41	43 48	37	39 5	6 9	36 33	57 15

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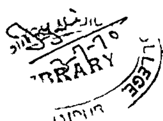
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By

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THE ARCHITECTURE OF THE TENDON

The tendon is a connective tissue structure composed of closely packed collagen fibers and protein mucopolysaccharide The collagen fibers are as long as the tendon (Bucher 1962) and where they do anastomose with each other they do so at acute angles The cell responsible for the elaboration of the collagen and the protein mucopolysaccharide and maintenance of the integrity of the tendon is the "Tenocyte or fibroblast (Hall M C 1965) The collagen fibres are grouped together in primary bundles (Schneider 1959) which in turn are assembled into larger secondary bundles (Schneider 1959) or fascicles (Edwards 1946) The secondary bundles then form tertiary bundles (Schneider 1959) which together comprise the tendon Tendons vary in length and in cross sectional area and the latter varies with the part of the tendon diminishing in a proximodistal direction Edwards (1946) claims that if the secondary bundles or fascicles are considered as the unit structure of tendon then some uniformity exists These fascicles are hexagonal in shape with a cross sectional area between 0 125–0 375 square millimeters

The tendon bundles are surrounded by a woven mesh of loose connective tissue the peritenoneum internum or endotenon This tissue holds the bundles together permits some movement of bundles with relationship to each other and carries all the blood vessels lymphatics and nerves It has elastic fibres (Hirai 1959) which tend to draw the tendon bundles into a wavy formation when relaxed At the musculotendinous junction there is an intimate relationship between the sarcomeres and the collagenous fibril bundles although no direct continuity exists (Boyd 1960) Electron microscopic studies have shown that the sarcolemma is intact at the junction and that the tendon bundles are invaginated into the ends of muscle fibers in the many terminal indentations of the outer sarcolemmal layer In this way a considerable surface contact between the muscle fiber and the collagenous fibrils is achieved Each group of muscle fibers enclosed in perimysium continues as a secondary bundle or fascicle and the peri

mysium is continuous with the endotenon (Edwards 1946) This very regular arrangement does not hold true where muscle fibers join the *tendon obliquely*, but the general organization pattern is similar

At the tendo osseous junction the collagen fibers continue as the perforating fibers of Sharpey The endotenon becomes continuous *with the periosteum* but the cortical zone of the bone at the insertion of the tendon, as long as the cross sectional area of insertion is not large is free of periosteum (Schneider 1959)

The whole tendon is surrounded by a fine connective tissue sheath, the peritenoneum externum or epitenon, which is continuous throughout on its inner surface with the endotenon

Surrounding the tendon is a loose fatty areolar tissue, *the paratenon* (Smith 1965) Its mechanical function is to allow the tendon to glide freely against the surrounding tissue (Brand 1961, Stanisavljevic 1962) In areas where a tendon passes over a structure which might harm it that is zones of local pressure and friction, the *paratenon* is replaced by a synovial sheath or bursa and in the tendon in corresponding areas either cartilagenous plates or sesamoid bones may develop The visceral layer of this tenosynovium is dense fibro elastic and closely adheres to the epitenon (Edwards 1946) The visceral and parietal layers of the tenosynovium are continuous with each other at the ends of the tendon synovial sheath as well as through mesentery like structures the mesotendons which in some areas have been designated as vincula tendinum

THE BLOOD SUPPLY TO THE TENDON

The tendon is a well vascularized tissue The blood supply is less profuse than that of muscle but there is no tendon without a blood supply (Biesalski and Mayer 1916 Smith 1965)

A tendon receives its blood supply *at the musculotendinous junction,* along its length whether it be in paratenon or tendon sheath and in the region of its insertion

A The Musculotendinous Junction

There are a number of longitudinal vessels, both arterial and venous which traverse *the musculotendinous* junction (*Wollenberg* 1905 Arai 1907 Rau 1914 Dychno 1936 Edwards 1946) Most of these vessels run in the depth of the tissues The observation of Rau (1914)

that vessels which in youth cross the musculo tendinous junction in the depth later in life assume a superficial position has not been substantiated by subsequent investigators Both Pau (1914) and Dychno (1936) made the observation that frequently one or two of these vessels appear as chief vessels and after crossing the musculotendinous junction traverse the full length of the tendon only to loop back on themselves at the musculo osseous junction

Edwards (1946) pointed out that only the vessels in perimysium continue into the tendon but that the capillary circulation of the muscle and of the tendon is completely separate and distinct The capillaries adjacent to the sarcomeres loop back at the musculotendinous junction to drain into the venules of the muscle and no capillary anastomoses exist at the junction of the two tissues

In addition to this longitudinal system one frequently encounters smaller arteries and veins which divide near the musculotendinous junction with one branch joining the muscle and the other the tendon

B The Paratenon

The paratenon contains many vessels which are largely responsible for the blood supply to the tendon (Wollenberg 1905 Arai 1907 Pau 1914 Dychno 1936 Edwards 1946 Smith 1965) At frequent intervals small vessels arise from neighbouring vessels and run transversely through the paratenon towards the tendon On approaching the tendon these vessels may branch several times before assuming a direction parallel with the longitudinal axis of the tendon It is at this point that they join the tendon circulation (Edwards 1946 Smith 1965)

C The Synovial Tendon Sheath

The synovial tendon sheaths have rich vascular nets on their surface as well as in their depths (Dychno 1936 Edwards 1946) These are more profuse in the areas of the pulleys (Smith 1965) The *visceral layer of the tenosynovium* receives a rich blood supply through the meso tendons as well as through its connections with the parietal layer at the ends of the synovial tendon sheaths (Edwards 1946) The meso tendons are nothing more than prolongations of the paratenon (Dychno 1936) although in this instance the paratenon is *interposed* between two layers of synovial tissue As in the paratenon the number of vessels in a particular region varies The *circulation* in the visceral layer of the tenosynovium (Edwards 1946 Observations made on the cow)

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The architecture of the epitenon vessels is very variable It is generally very profuse in areas where the tendon is in paratenon but varies not only from tendon to tendon but also in different areas of the same tendon Certain areas of the epitenon have a highly characteristic and organized vascular architecture (Guse 1963 Winter 1965) No epitenon vessels are located on the side of the tendon which comes in contact with pulleys or where friction would be at its maximum (Smith 1965) An excellent example of this is the arrangement of the vincula tendinum on the dorsum the nonfriction area of the tendons within a tendon sheath

THE METABOLISM OF THE TENDON

A co relationship exists between the blood supply of a tissue and its metabolic requirements The information on tendon metabolism however is very scanty Neuberger (1953) measured a small but definite turnover of amino acids in the collagen of adult tendons and Peacock (1959) found the respiratory activity to be 0 1 microliters per unit weight per hour

White (1964) has estimated the average rate of blood flow in tendon to be 0 10 cubic centimeters per gram per minute The contentions of Berkenbusch (1887) and Rau (1914) that the blood supply in tendon varies with age have found some confirmation in the experiments of Rothman (1965) who found that there is an apparent decrease in the capillary bed of a tendon with aging More recently Rothman (1967) has also demonstrated that a significant decrease occurred in the capillary bed volume in tendon tissue following a six week period of immobilization

THE INVESTIGATION

No intravital study of the microvascular anatomy and microcirculation of the tendon could be found in the literature

All studies published to date have been carried out on dead specimens The vessels of the tendons prior to study were usually filled with a contrast medium The tendon was then in accordance with the technique employed suitably processed and examined microscopically or by angiography Such an approach has certain obvious inherent draw

consists of a superficial capillary network and a much deeper plexus of arteries and veins The capillaries loop to the surface from the underlying arterioles and venules It is only the deep plexus which communicates with the tendon circulation" by short anastomotic channels

D The Tendon Bone Junction

Wollenberg (1905), Arai (1907) Rau (1914) Dychno (1936) and Nichols (1954) were unable to demonstrate any direct communication between the tendon circulation and bone They all describe anastomoses between the tendon vessels and periosteum Only Edwards (1946) claims to have been able to demonstrate in some areas branches passing directly through to the cortical layers of bone but he also points out that these vessels are small, few and irregularly distributed

The vessels in the tendon at its insertion anastomose with those present in the periosteum and only by means of this indirect communication have a connection with the osseous circulation

The arrangement of the internal vascular architecture of the tendon is primarily one of longitudinally oriented blood vessels which run in the endotenon in the long axis of the tendon (Arai 1907, Biesalski and Mayer 1916, Dychno 1936, Edwards 1946 Braithwaite and Brockis 1951, Brockis 1953, Smith 1965)

According to Edwards (1946) these vessels are arteriolar in size with a well developed tunica media and are arranged around the fascicles Accompanying each arterial channel are two veins one on each side which communicate frequently with each other usually in the neighbourhood of a tributary or a branch (Edwards 1946 Brockis 1953) Dychno (1936) on the other hand, found only occasionally larger vessels Most of the vessels he was able to demonstrate histologically were capillaries with a single endothelial lining

The capillaries arise from the arteriolar branches, form loops which then drain into several venules These loops may run from one longitudinal channel to another or back to the parent vessel The capillaries are intra fascicular and do not penetrate the collagen bundles (Dychno 1936 Edwards 1946)

This internal vascular system is fed from the vessels present in the epitenon Branches arise from the epitenon vessels and enter the tendon substance radially along the endotenon These either anastomose directly with the longitudinal vessels or divide first into ascending and descending branches before doing so

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MATERIAL AND METHODS

50 young rabbits (2–3 months of age) weighing approximately one kilogram were employed in this investigation

Part I Microangiography and india ink injections

Microangiography was carried out as described by Lundskog and Branemark (1968) India ink injections were carried out with commercially available india ink diluted with normal saline in the ratio of 1 3 and then filtered six times through Munktell filter paper No 3 No measurements of injection pressures were carried out Before injection the animal was heparinized Injections were carried out through the femoral artery aorta and where special emphasis was placed on the front paw through a polyethylene canula inserted into the axillary artery After perfusion with Micropaque® or india ink the animal was given an overdose of anaesthetic and then the whole animal was immersed in 10% formalin for 10 days

Tendons subjected to microangiography were carefully prepared by micro-dissection to preserve the epitenon Tendons injected with india ink were carefully dissected out preserving the paratenon periosteum and muscle The tendons were then cleared using the Spalteholz technique and while immersed in the clearing solution with the aid of the stereo dissecting microscope (Leitz) were carefully prepared with micro instruments to preserve the architectural pattern of paratenon and epitenon Recordings were made with the Leitz Wetzlar camera using objectives 16 mm 1 2 5 25 mm 1 3 5 and 63 mm 1 4 5 with variable intensity diffuse transillumination and variable diaphragm openings of the objectives to allow for adjustment of focal length and thus allow for different degrees of optical tissue penetrance

Part II Intravital Microscopy

All animals were anaesthetized using intravenous urethane and were tracheotomized An attempt was made to carry out the intravital observations under as ideal conditions as possible (Branemark 1959) All preparations were carried out using microsurgical techniques with the aid of variable magnification and filtered illumination with the infra red portion of the spectrum filtered out Hemostasis was achieved either by application of saline soaked Spongostan® or with a micro diathermy unit (Brånemark 1964)

backs The accuracy of the study depends on the degree of successful filling of the microvascular system with the injection medium An even greater disadvantage of these techniques is that they do not provide any information on the haemodynamics of the microcirculation One *can demonstrate a vessel but one must infer its function* The behaviour of the microvascular units during physiological function of the tissue they are in cannot be studied at all

In recent years there has been an attempt to define the relative importance of the blood vessels reaching the tendon Peacock (1959) on the basis of radioactive isotope (P^{32}) uptake concluded that "the blood vessels entering long tendons from the muscular origin and periosteal insertion are able to nourish only the proximal and distal third of the tendon The intrinsic vessels in long tendons are not capable of nourishing *the central third by anastomoses with vessels entering from either end* Circulation to the central third of long tendons is by intermediate segmental vessels entering through disorganized paratenon or a definite volar mesentery Permanent disruption of the central blood vessels to normal tendons or mechanical prevention of post operative adhesions around free grafts, causes cellular death and eventual disintegration of collagen bundles' Smith in 1965 delineated the segmental nature of the blood supply more precisely He stated on the basis of silicone rubber compound injections that the micro circulation in tendons is *segmental in nature and that a tendon freed from its segmental blood* supply will only survive over a distance of 1–2 cm from its intact circulation This conclusion however was based on the mere demonstration of vessels without an assessment of their function

The recent advances in intra vital microscopy allow for analysis of tissues and cells to proceed at a resolving level of 0 5 μ and some times even better (Branemark 1966) Thus it is possible to observe simultaneously the microvascular system and the structure and function of the living tissue within which the microvascular system is found It is possible to study the intricate and intimate relationship between capillary structure capillary topography and flow pattern and how this structure and activity of the terminal vascular bed is organized to meet the metabolic needs of the tissue

The present investigation was designed in two parts Part one was devoted *to an assessment of the accuracy* of morphologic demonstrations of the microvascular system of the tendon by means of clearing tech niques and microangiography Part two was devoted to intravital observa tions on the microvascular anatomy and microcirculation of the tendon

The lack of any uniformity in the vascular architecture of the epitenon circulation in different tendons and even in the same tendon was striking (See Fig 4 and compare it with Fig 2 and 3) Fig 5 and Fig 6 are segments of the same tendon showing an entirely different arrangement of the epitenon vascular architecture

An attempt was made to analyze the relationship between the tendon mass and the spacial orientation of the vessels In order to accomplish this we analyzed cross sections of thin flat tendons such as the extensor digitorum communis distal to the musculotendinous junction but proximal to the extensor retinaculum and thick round tendons such as the flexor carpi ulnaris A definite correlationship was established Thick round tendons in addition to their epitenon circulation have a number of vessels deeply situated in their substance (See Fig 7 8 and 9) In many instances it was possible to demonstrate the connections between the epitenon vessels and those in the substance of the tendon (See Fig 9 10 and 11) Thin flat tendons on the other hand have most of their vessels situated either in epitenon or very close to the surface in endotenon (See Fig 12 and 13)

Part II Intravital Microscopy

A number of tendons were examined before the extensor digitorum communis was chosen as the experimental model These trials will be discussed because observations made during the search for a suitable tendon and a suitable method are pertinent to the discussion The first tendon to be examined was the tendo achilles Although attempts at transillumination failed because of the thickness of the tendon under the dissecting microscope at a magnification of 80× we observed a very rich epitenon circulation characterized by very similar repeating microvascular units fed by separate arterioles and draining into separate venules We transsected the tendo achilles at its mid and lower third with a micro scalpel and used microdiathermy to control hemorrhage from the epitenon circulation We found many punctate hemorrhages in the depth of both the proximal and distal stumps which confirmed the presence of vessels within the tendon

The next tendon to be examined was the tibialis anterior In the rabbit the parietal tenosynovium surrounding the tibialis anterior at the ankle forms a large sac and contains a considerable quantity of synovial fluid The extensor retinaculum is in the form of a thick fibrocartilageous band We chose this tendon to avoid the problems

The exposed tendons were studied in the 'Leitz Intravital Micro scope using both transillumination and incident illumination For incident illumination the Ultropak objectives UO×3 8×6 5×11 and ×22 were employed Photomicrographic recordings were made as described by Branemark (1963) and with certain modifications thereof

RESULTS

Part I A Microangiography

Microangiography proved to be an unsuitable method for the dem onstration of tendon micro vascular architecture In spite of constant perfusion conditions the filling of the vascular system with Micropaque was very variable In addition the kV and mA required for uneven tissues, burned out" in some areas any microvascular portion of the system that was filled These tendons were subsequently cleared by the Spalteholz technique and examined A very variable filling of the small vessels was observed with frequent embolic' phenomena An attempt was made to use "Thorotrast" instead of Micropaque Although the study was carried out only in one animal the necessity for immediate removal of the tendon with ensuing leakage of the 'Thorotrast from patent vessels does not suggest great promise for this technique

B India Ink Injections

With this method it was possible to achieve a much better filling of the micro vascular system and more reliable studies could be ac complished It must be emphasized, however, that despite filtering of the solution and heparinization of the animal when such a perfusion was observed under the intravital microscope frequent clumping with embolic phenomena occurred This resulted in a variable filling of the microvascular system Even if intravascular clumping of the particles did not occur then only those capillaries were filled which were open while the perfusion was being carried out Therefore we did not attempt any detailed analysis of the microvascular system on the basis of this method It was employed as a means of general survey of the vascular anatomy of the tendon in the rabbit

The illustrations (Fig 1 Fig 2 and Fig 3*a b*) show that the vascular anatomy of the tendon in the rabbit conforms to the general pattern observed in man

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An attempt was made to analyze the relationship between the tendon mass and the spacial orientation of the vessels In order to accomplish this we analyzed cross sections of thin flat tendons such as the extensor digitorum communis distal to the musculotendinous junction but proximal to the extensor retinaculum and thick round tendons such as the flexor carpi ulnaris A definite correlationship was established Thick round tendons in addition to their epitenon circulation have a number of vessels deeply situated in their substance (See Fig 7 8 and 9) In many instances it was possible to demonstrate the connections between the epitenon vessels and those in the substance of the tendon (See Fig 9 10 and 11) Thin flat tendons on the other hand have most of their vessels situated either in epitenon or very close to the surface in endotenon (See Fig 12 and 13)

Part II Intravital Microscopy

A number of tendons were examined before the extensor digitorum communis was chosen as the experimental model These trials will be discussed because observations made during the search for a suitable tendon and a suitable method are pertinent to the discussion The first tendon to be examined was the tendo achilles Although attempts at tran illumination failed because of the thickness of the tendon under the dissecting microscope at a magnification of 80× we observed a very rich epitenon circulation characterized by very similar repeating microvascular units fed by separate arterioles and draining into separate venules We transected the tendo achilles at its mid and lower third with a micro scalpel and used microdiathermy to control hemorrhage from the epitenon circulation We found many punctate hemorrhages in the depth of both the proximal and distal stumps which confirmed the presence of vessels within the tendon

The next tendon to be examined was the tibialis anterior In the rabbit the parietal tenosynovium surrounding the tibialis anterior at the ankle forms a large sac and contains a considerable quantity of synovial fluid The extensor retinaculum is in the form of a thick fibrocartilageous band We chose this tendon to avoid the problems

of the paratenon and hoped that in this fashion a segment of the tendon could be transilluminated with its internal vascular supply" intact The synovial tendon sheath and the fibrocartilagenous extensor retinaculum were opened The tibialis anterior was transilluminated with its insertion intact as well as transsected at its insertion and lifted out of its bed We again failed to visualize any internal vascular supply This undoubtedly is related to the thickness of the tendon the relatively poor contrast of living unstained tissues and the inability to penetrate optically a thick translucent tissue with the intravital microscope

The surface of the tendon deep to the extensor retinaculum, was devoid of any vessels at the level of the ankle joint as this is a friction zone A mesotendon reached the tibialis anterior on its posterior non friction surface This afforded an opportunity to observe the circulation in the mesotendon as well as in the epitenon on that side

The mesotendon contained vessels of the order of pre arteriolar arteries and small veins The mesotendon was long and the vessels folded up in an accordion like fashion without any disturbance in the flow of blood Stretching the mesotendon first produced a slowing of both the arterial and venous circulation and at greater tensions the circulation came to a standstill On reaching the epitenon the arterial vessel divided into a central ascending and descending branch from which at regular intervals on both sides arose arterioles which in turn gave rise to capillary beds Each capillary bed drained towards the central vessel via many venules which on reaching the center gave rise to one or two venae comitantes one on each side of the arterial vessel The capillary circulation had also many capillary anastomoses at its periphery joining each microvascular unit with its neighbour Occasionally one could also see a branch of an arteriole dipping into the substance of the tendon

The extensor carpi ulnaris was chosen as the next *tendon* Because of its situation once the paratenon was stripped the tendon could be easily lifted out of its bed and by rotating the limb one could easily bring this tendon between the condenser and the objective of the microscope This tendon was thin There was no problem with transillumination or optical penetration of the tissue Yet we failed to identify a single vessel except in the region immediately adjacent to the musculotendinous junction where *the circulation* appeared intact

The extensor digitorum communis is a long flat tendon which only narrows and becomes round close to the extensor retinaculum In its proximal portion immediately adjacent to *the musculotendinous*

junction to the naked eye it appeared as a single tendon Under the dissecting microscope however, even at this level four discrete tendons thin and flat all enveloped in a glistening transparent paratenon could be identified More distally the identity of each tendon become more obvious These tendons are so arranged that in their proximal portion they slightly overlap each other with the most lateral (radial) one being most superficial

A window was made in the lateral aspect of the paratenon and a prism 1 mm×1 mm and 3 mm in width attached to a fibre optic was introduced under the tendon In this way transillumination of a tendon in paratenon could be achieved (See Fig 14)

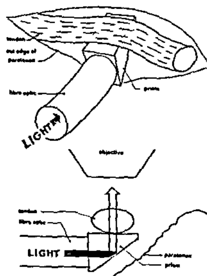


Fig 14 Illustration of transillumination of a tendon with a fibre optic and prism

Only large arterioles and venules could be demonstrated The circulation was obviously impaired The preparation was very sensitive to the extent the paratenon had to be freed to allow for the introduction of the prism under the tendon and also to the stretching of the tendon over the edge of the prism The prism was modified A plexiglass rod was employed (See Fig 15) The end was ground to a flat disc 5 mm in diameter and 1 mm in height In the center a groove was cut 3 mm

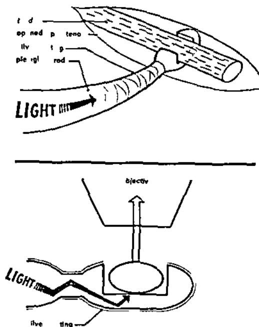


Fig 15 Illustration of transillumination of a tendon with a ground plexiglass rod

wide and ½ mm deep By manipulation the freed tendon was slipped into the groove and transilluminated Again only arterioles and venules with grossly impaired circulation could be demonstrated We observed, however that in incident illumination with most of the paratenon intact, a rich capillary circulation was present in the tendon This observation led to the development of our present experimental model

The paratenon and perimysium were carefully removed by means of microdissection from the exposed surface of the tendon and muscle respectively preserving every vessel The specimen was examined in incident light illumination with the ultropak equipment (See Fig 16)

We observed long and tortuous vessels in the paratenon interposed between the deep fascia and the tendon as well as paratenon vessels which reached the tendon from the side and on its under surface These paratenon vessels were both arterial and venous The arterial vessels on reaching the tendon divided first into smaller vessels which then give rise to a capillary plexus (See Fig 17) Our area of observation was limited to the musculotendinous junction and to the flat portion of the tendon Where the tendon become round and passed beneath the extensor retinaculum it was in tenosynovium and had no surface vessels present as this is a friction zone

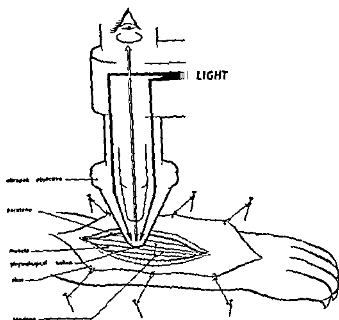


Fig 16 Illustration showing the method of intravital observation of the tendon circulation using incident illumination

A The Musculotendinous Junction

Observations carried out on the musculotendinous junction have disclosed the following (See Fig 5)

(1) The microvascular architecture of the muscle and of the tendon differ not only in their pattern but also show no communication The muscle capillaries run a straight course along the sarcomeres (See Fig 18) and where these join the tendon the capillaries loop back to rejoin the muscle circulation (See Fig 19)

(2) There are a number of vessels which cross the musculotendinous junction These vary in size are quite superficial and are both arterial and venous although the veins do appear to be predominant

B The Tendon in paratenon

There were a number of longitudinal vessels which ran in the long axis of the tendon Unfortunately most of these were too deep to be resolved with any detail using incident illumination Flow directions

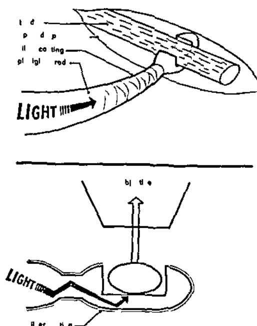


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capillary
venule
capillary
arterioles
arteriole
vein
vein

arrows



indicate direction of flow in larger vessels
indicate direction of flow in capillaries and venules

[illegible] Diagram ill trat g the long loop c llary pattern in t n l n

in these vessels were both proximal and distal, but on this basis alone it was impossible to conclude which was arterial and which was venous

Arterioles appeared in random fashion close to the surface of the tendon and gave rise to the following types of microvascular units

(1) There were capillary loops which ran for long distances parallel to the tendon bundles then looped back, traversed an even longer distance again parallel to the tendon bundles before looping back again to join a venule One arteriole gave rise to more than one capillary loop, and by focusing up and down, it was possible to discern that these were in different planes of the tissue (See Fig 20 and Fig 21)

(2) There were regions where the microvascular architecture appeared to be less specialized and resembled that of the hamster s check pouch (See Fig 22 and Fig 23)

(3) There were also regions where the capillaries were very short, ran a straight course and immediately joined a venule This suggested that they may function as shunts

In all capillaries (See Fig 24), high flow velocities have been observed The velocities were so great that erythrocytes could not be identified as discrete particles with visual observation This suggested a flow velocity of at least 1 0–1 5 mm/sec Reversal of flow in the capillaries has been observed as well as vasomotion

We subjected the tendon circulation to a number of manipulations

Trans section of the Tendon at the Level of the Carpus

(1) Once the tendon was cut, it immediately assumed a wavy pattern but no observable changes took place in its circulation in the exposed re gion which was being continuously observed

(2) *Trans section of the Tendon at its Musculotendinous Junction*

This manouver was associated with considerable hemorrhage The circulation in many of the longitudinal vessels stopped but the regional capillary circulation except that immediately adjacent to the cut appeared unaffected

(3) *Isolation of a Segment of Tendon by Proximal and Distal Trans section Maintaining the Paratenon Intact*

Immediately following the trans section all circulation in the tendon often came to a stand still In some areas pulsatile movement of the

capillary

venule

capillary

arterioles

arteriole

vein

vein

arrows

indicate direction of flow in larger vessels

indicate direction of flow in capillaries and venules

Fig. [illegible]. Diagram illustrating the long loop capillary pattern in tendon



blood column occurred Within one to two minutes however most of the arteriolar, capillary, and venular circulation in the isolated segment of tendon was resumed often sluggishly at first, but it soon returned to its former vigour (See Fig 25)

(4) *Trans section of the Tendon Distally and Application of Varying Degrees of Tension*

As previously stated distal trans section had no influence on the circulation proximally As greater and greater tension was applied changes could be observed At first the venous circulation slowed down then the capillary, until finally flow ceased altogether On releasing the tension the flow was immediately resumed

(5) *Tendon Lymphatics*

We have attempted to repeat Edwards (1946) method of lymphatic channel demonstration He cautioned that the preparation must be fresh to succeed Our preparation was alive We observed all the technical points, and yet failed to get a single preparation

In addition methylene blue was deposited in the tendon distally in the hope that with time and exercise the dye would be taken up by the lymphatics Up to six hours no dye was observed proximally in the tendon

DISCUSSION

The literature abounds with the term 'The Blood Supply to Tendons" without regard to the tendon in question Berkenbusch (1887) studied the flexor tendons within flexor sheaths Rau (1914) based his observations on the infrapatellar tendon and the tendo achilles Edwards (1946) studied the flexors and extensors crossing the metacarpals and metatarsals Arai (1907) Dychno (1936) and Smith (1965) have studied the tendons in the whole extremities Similarities do exist but it is only on similarities that generalizations can be based

There are many variations in the arrangement of vessels even within a single tendon which have to be considered if a meaningful functional analysis of tendon circulation is to be established

It is important to draw clear distinction between endotenon epitenon tenosynovium and paratenon because this not only gives precise anatomic localization but also identifies regions of the tendon subjected to different local mechanical situations which determine the manner of the

blood supply to the tendon Thus in paratenon where the relative amplitude of displacement of the tendon in relationship to the immediately adjacent tissue the paratenon is negligible because the paratenon moves with the tendon vessels can reach the tendon in a random fashion where the relative amplitude of displacement of the tendon in relationship to the immediately adjacent tissue is great because the tissue is fixed such as a pulley an a retinaculum or fibrous tendon sheath the blood vessels reach the tendon on its non friction side in a specialized structure the mesotendon Although we have found the injection techniques not sufficiently accurate for the demonstration and study of the microvascular units they serve well for the demonstration of larger vessels and for the study of their spacial organization On the basis of our injection studies we have demonstrated that the spacial organization of blood vessels of tendons is related to the size of the tendon Thin flat tendons tend to have most of their vessels arranged superficially in epitenon whereas thick round tendons have both a superficial and a deeper internal blood supply It is for this reason that we feel that the epitenon circulation cannot be divorced from the tendon circulation proper because it takes part in supplying the metabolic needs of the tendon This superficial and deep arrangement of vessels also suggests that there must be a critical distance between a microvascular unit which is the metabolic exchange zone and the tenocyte or that there is a relationship between a specific mass of tendon tissue and the spacial orientation of the microvascular units As yet we have been unable to define this relationship but feel that the concept of Edwards (1946) and Prockies (1953) of a simple uniform system of vessels throughout with frequent and regular cross anastomosis is a gross over simplification We have demonstrated in vivo three types of microvascular units which are not evenly or constantly distributed The function of the longitudinal intrinsic vessels still remains obscure They are incapable of supporting long segments of tendon whether it is in paratenon or tendon sheath (Potenza 1959 Peacock 1963 Smith 1965) We have not been able to observe any circulation in the longitudinal vessels of tendons completely stripped of their paratenon blood supply In tendons with only partially disrupted segmental paratenon blood supply the circulation in the longitudinal vessels was impaired In an isolated segment of tendon with the paratenon vessels intact the microvascular circulation was intact but the flow in the longitudinal vessels was interrupted This would suggest that they may be only venous channels and for this reason of course are unable to maintain a tendon viable

which has been isolated from its segmental arterial blood supply

The fact that the blood supply to tendon is segmental may have definite bearing on certain clinical therapeutic manouvers Branemark et al (1967a b), and Goldie (1967) showed that certain suspension media of corticosteroids completely arrest capillary blood flow One of the authors (J S) has knowledge of two patients whose tendoachilles were injected for crepitant tenosynovitis Within two weeks the patients sustained spontaneous ruptures of their tendo achilles It is likely that local necrosis of the tendo achilles occurred and as this tendon has to withstand tremendous tensile stresses, it ruptured in the necrotic area

We have adequate data to dispel certain long held concepts in tendon surgery Hall (1965) writes There is some purpose in distinguishing between a tendon transfer in which vascularized tendon is moved from its normal point of attachment and inserted into an adjacent area and tendon transplant in which the whole tendon is made avascular

Every manouver which separates the tendon from its segmental paratenon or mesotendon renders the tendon avascular This not only explains why adhesion formation occurs but also why blocking interposition substances are doomed to failure In tendon transfer sharp angulation point pressure and excessive tension must also be avoided for they embarrasses the tendon circulation

Intravital observations in incident light are limited to the superficial layers of tendon only Thus only the micro vascular units in the epitenon and in the most superficial layer of the tendon could be studied However as the epitenon circulation is part of the blood supply to the tendon and in thin flat tendons such as the one studied most of the vessels were disposed superficially we employed this technique as a biological window into the behaviour of the micro vascular system of the tendon

Our data on the micro vascular anatomy of the tendon is not adequate to allow for any further conclusions We have established an experimental model and have made certain *preliminary observations*

We are continuing our investigations and hope to present in the future a more comprehensive analysis of tendon circulation

SUMMARY

1 A review of the literature dealing with tendon circulation is presented
2 Different techniques for the study of tendon circulation are evaluated

3 A method for the intravital study of tendon circulation is presented

4 Conclusions

a) Injection techniques are not adequate for the study of the micro vascular units of tendon circulation

b) There must be a critical ratio between available micro vascular exchange surface area and mass of tendon tissue

c) The blood supply to tendons is segmental whether the tendon is in paratenon or tenosynovium

d) Any surgical manoeuver which frees the tendon from its paratenon or mesotenon devitalizes that segment of the tendon

e) The possible relationship between spontaneous tendon rupture and corticosteroid injection is presented

f) The influence of tension and compression on the tendon circulation is evaluated

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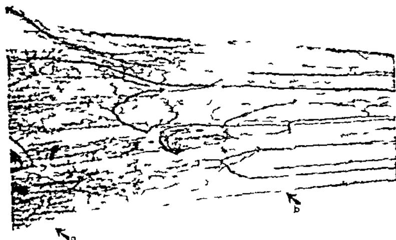


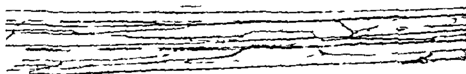
Fig. 1 Th m sc l ten l nous jun tion Extensor d git rum commun s Muscle and t n l l lij to long st toe Observe the following (i) The number of longitu l nal vessels f r ll l amet r wh ch trav rse the musculotend nous junct on (ii) The d screte l p i g ba k f ap ll ries supplying the sarcom res (iii) The strik ng difference i the n u l r f essl pr sent n muscle an l tendon (iv) Th diff rent ar hit ctural arrange t f ss l in th n uscle and those in the tendon (a) muscle (b) t n l n
Magn ficat on ×73



Fig. 2 S k s t f the same t t l s n in Fig. 1 w th preserved parat non vessel (a) j i ing the rcul t n f the ten l n Observe also the gen ral arrangement of the vessels the t n l on wh h conf rms t that pre u ly described in man Magn fication ×73

F... ... ...t n n ... e mn ... Observe the arrangement of th... p t n n ... vessel ... t d tal t th... vascul t n l ou ... n t ... n At arrow preserved paratenon vessel ... ar... l t Magnif... t n ... 20

F... ... t t ... Segment proximal to the tran... se carpal ligament ... the ... vasculature (arrow) and how it differs from Fig 5 Under the ... g m ... it was possible to follow vessels from this profuse ... ten n ... the length of th... t n Magnification 3



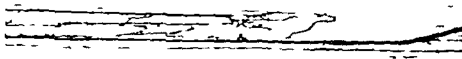


Fig 3*a*) & *b*) Different segments of the extensor digitorum communis tendon taken proximal to the extensor retinaculum Again observe the similarity in the architectural arrangement of the vessel (*a*) & (*b*) are arranged in a proximo distal order Magnification ×15

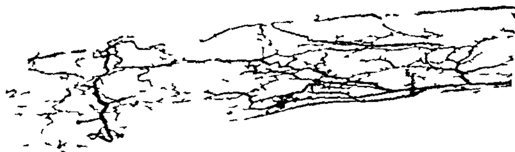


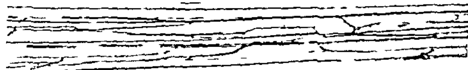
Fig 4 Extensor digitorum communis Segment in the region of the extensor hood Picture focussed on the superficial vessels Magnification ×15



[illegible] Observe the arra[illegible]ment of the ep[illegible]ten[illegible] vessels [illegible] ction. At arrow [illegible] present[illegible] paratenon vessel [illegible] Magnification [illegible]0



[illegible] Segm[illegible] proximal to the tran[illegible] carpal ligament [illegible] vascul[illegible]ture (arrow) and how it [illegible] Fig. 5 [illegible] from th[illegible] the [illegible] Magnification [illegible]3



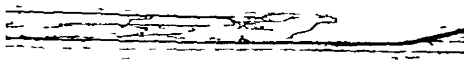


Fig 3(a) & (b) Different segments of the extensor digitorum communis tendon taken *proximal to the extensor retinaculum Again observe the similarity in the architectural* arrangement of the vessels (a) & (b) are arranged in a proximo distal order
Magnification ×15



Fig 4 Extensor digitorum communis Segment in the region of the extensor hood
Picture focused on the superficial vessels Magnification ×15

F g. 9 Cro section of a thick tendon. Photograph taken at a slightly oblique angle. Observe (a) the epitenon vessels (b) the preserved paratenon vessels ( ) the connections between the epitenon and the deeply situated vessels. Magnification × 0



Fig. 10 Sagittal section of a thick round tendon. Observe the epitenon vessels (a) and the ramifying vessels in the depth of the tendon (open arrows). Magnification 3

Fig 7 Cross section of a thick round tendon demonstrating the presence of vessel deeply situated in the substance of the tendon Magnification ×30

Fig 8 Cross section of a thick round tendon demonstrating the presence and ramification of vessel deeply situated in the substance of the tendon Note also the epitenon vessels (arrows) Magnification ×30

Fig. 9 Cross section of a thick tendon. Photograph taken at a slightly oblique angle. Observe (a) the epitenon vessels (b) the preserved paratenon vessel (c) the connections between the epitenon and the deeply situated vessel. Magnification × 0



Fig. 10 Sagittal section of a thick round tendon. Observe the epitenon vessels (a) and the ramifying vessels in the depth of the tendon (open arrows). Magnification 23

Fig 7 Cross section of a thick round tendon demonstrating the presence of vessels deeply situated in the substance of the tendon Magnification ×30

Fig 8 Cross section of a thick round tendon demonstrating the presence and ramification of vessels deeply situated in the substance of the tendon Note also the epitenon vessels (arrows) Magnification ×30

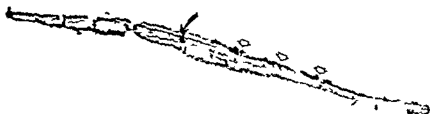
Fig. 9 Cross section of a thick tendon Photograph taken at a slightly oblique angle Observe (a) the epitenon vessels (b) the preserved paratenon vessel (c) the connections between the epitenon and the deeply situated vessel Magnification ×2?



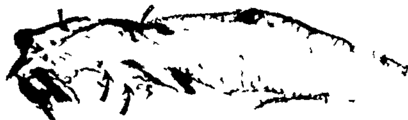
Fig. 10 Sagittal section of a thick round tendon Observe the epitenon vessels (a) and the ramifying vessels in the depth of the tendon (open arrows) Magnification ?3

Fig 7 Cross section of a thick round tendon demonstrating the presence of vessels deeply situated in the substance of the tendon Magnification ×30

Fig 8 Cross section of a thick round tendon demonstrating the presence and ramification of vessels deeply situated in the substance of the tendon Note also the epitenon vessels (arrows) Magnification ×30



F g 1 Cro s section of thin flat xtensor digitoru n commu s ten lon The l lack d ts are the vessels in cross sect on (open arrows) There is only one v ssel in th d pth of th t lon (l sed ar ow) and eve i this one is close to the urface Magn fication × 50



F g 13 Cros secti n of xtensor d gitorum communis tendon closer to the extensor retinaculum where the ten lon becomes th cker and round Note the appearance of vessels n its depth (arrows) M gnification × 65

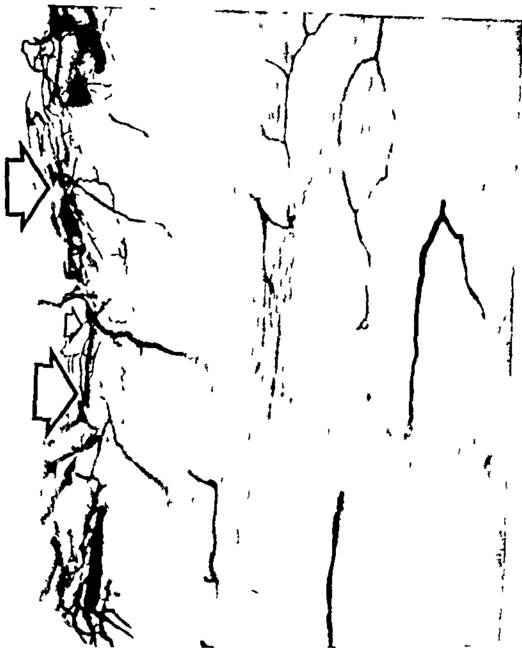


Fig 11 Sagittal section of a thick round tendon Note the connection between the epitenon and endotenon vessels (open arrows) Magnification ×50

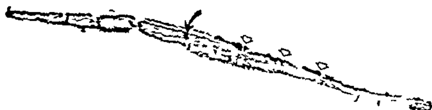


Fig 1 Cross section of thin flat extensor digitorum communis tendon The black dots are the vessels in cross section (open arrows) There is only one vessel in the depth of the tendon (closed arrow) and even this one is close to the surface Magnification × [illegible]

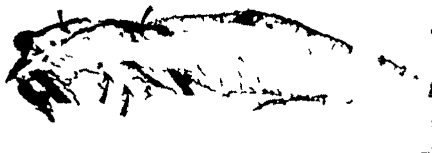


Fig 13 Cross section of extensor digitorum communis *tendon closer* to the extensor retinaculum where the tendon becomes thicker and round Note the appearance of vessels in its depth (arrows) Magnification × 6[illegible]



Fig. 11 Sagittal section of a thick round tendon Note the connection between the epitenon and endotenon vessels (open arrows) Magnification × 50

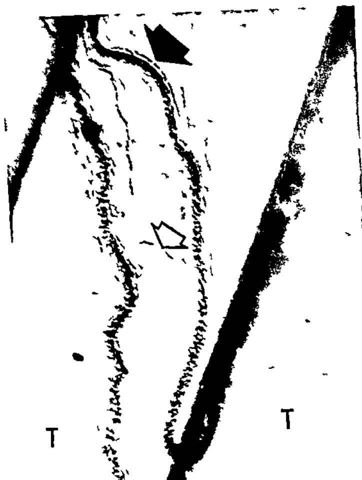


Fig 1 Note a capillary (open arrow) from the tendon (T) draining into a paratenon vein (closed arrow) Intravital photograph Magnification ×125

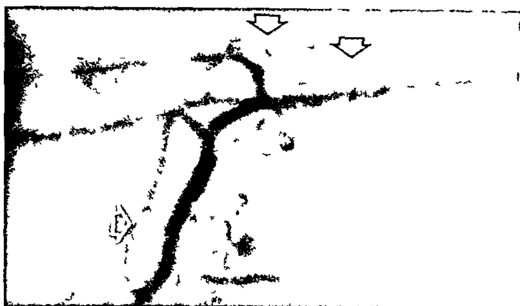


Fig 17 The Paratenon Vessels

Fig 17*a* Note that upon reaching the tendon the paratenon vessels (white arrow) divide giving rise to progressively smaller vessels until a capillary plexus is formed (open arrows) Intravital photograph Magnification ×100

Fig 17*b* Note that the large vessels (closed arrow) are in paratenon and run in this tissue between tendons Arterioles arise from the paratenon vessel when it is still large (open arrow) and go directly to the tendon Intravital photograph Magnification ×100

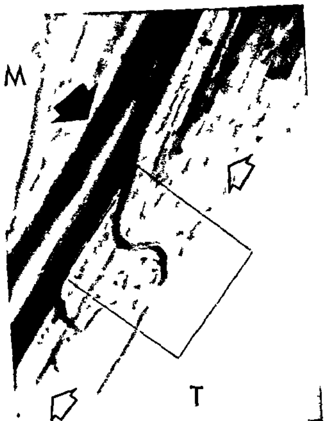


Fig 19 The musculotendinous junction

Fig 19a Note that the capillaries which supply the sarcomeres (open arrows) loop back and that there is no capillary anastomosis between muscle and tendon The larger vessels (closed arrow) traverse the musculotendinous junction and continue into the tendon Muscle—M Tendon—T Area in square magnified—see 19b Intravital photograph Magnification ×150

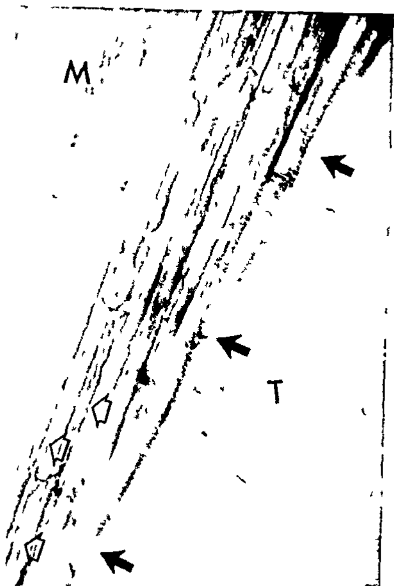


Fig 18 The musculotendinous junction Muscle M Tendon T Note that the muscle capillaries (open arrows) run along the sarcomeres Note also the sharp separation between muscle and tendon (closed arrows) Intravital photograph Magnification ×215

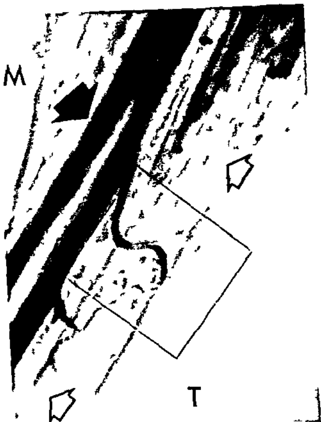


Fig 19 Th musculotendinous junct on

F g 19*a* Note that the cap ll ries wh ch supply tl e sarcomeres (open arrows) loop back and that th re is no cap llary anastomos s between muscle and tendon The larger essel (closed arrow) tra erse the musculotendinous junction and continue into the tendon M scle—M Tendon—T Area in square magn f ed—see 19*b* Intravital photo graph Magnif cat on ×150

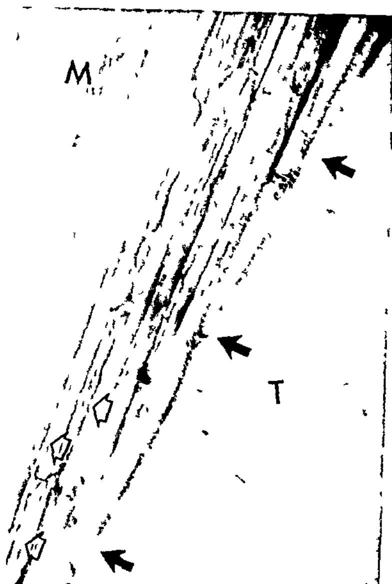


Fig 18 The musculotendinous junction Muscle M Tendon T Note that the mu cle capillaries (open arrows) run along the sarcomeres Note al o the sharp separation between muscle and tendon (closed arrows) Intravital photograph Magnification ×275



F 1 In tr tal photograph of th l ng loop pillary pattern in tendon Open arrow—
I ll ry Closed arrow —a t ri l T—tendon Magnification ×100

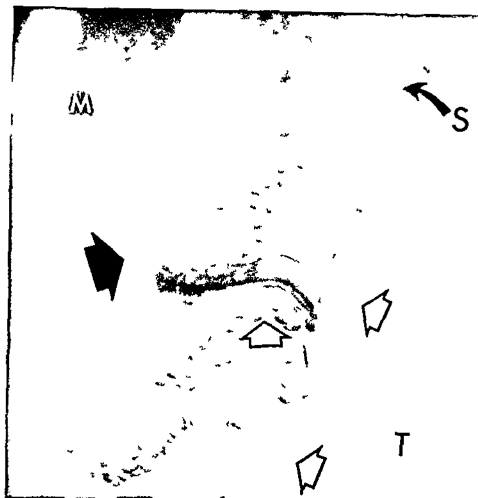


Fig 19b Note the arteriole in perimysium (closed arrow) giving rise to capillaries (open arrows) which supply the sarcomeres There is no capillary anastomosis between the muscle (M) and tendon (T) the two capillary systems being quite separate Note also the cross striations in the sarcomere (S) Intravital photograph Magnification 500

E

R

Fig. 4. T[illegible] capillary. Observe the discrete endothelial lining of the capillary (E) [illegible] row of erythrocytes (R). Intravital photograph. Flow rate slightly reduced. Magnification × [illegible]

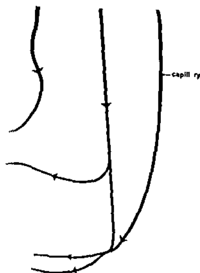


Fig 22 Diagram illustrating the less specialized microvascular unit in tendon

Fig 23 Intravital photograph illustrating the less specialized microvascular units (open arrows) in tendon—T Magnification ×*100*

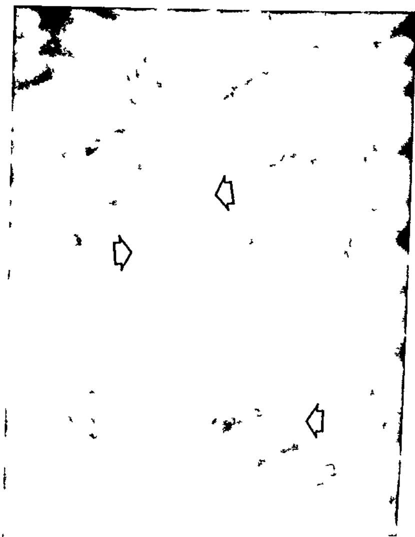


Fig 25 Isolated segment of tendon with its circulation preserved Note the waviness of the tendon This waviness appears immediately upon proximal or distal transection of the tendon The vessels (open arrows) are not well demonstrated because of the different focal planes they assumed due to the waviness Magnification × 100

CORTICAL BONE HEALING

A METHOD OF MEASURING THE CHANGE IN COMPRESSION APPLIED TO LIVING CORTICAL BONE

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F Straumann M E. Muller & M Allgower

THE REACTION OF CORTICAL BONE TO COMPRESSION

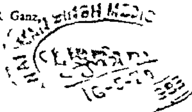
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A DYNAMIC COMPRESSION PLATE

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CLINICAL EXPERIENCE WITH A NEW COMPRESSION PLATE DCP

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GÖTEBORG 1969
ELANDERS BOKTRYCKERI AKTIEBOLAG

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FROM THE LABORATORY FOR EXPERIMENTAL SURGERY
SWISS RESEARCH INSTITUTE
DAVOS SWITZERLAND
(Stephan M Perren head)

A METHOD OF MEASURING THE CHANGE IN COMPRESSION APPLIED TO LIVING CORTICAL BONE

by

S M Perren A Huggler M Russenberger
F Straumann M E. Muller and M Allgower

with the technical assistance of V Geret and M Klebl

A METHOD OF MEASURING THE CHANGE IN COMPRESSION APPLIED TO LIVING CORTICAL BONE

INTRODUCTION

Continuously changing mechanical stress seems to be essential for the maintenance of the functional internal architecture of a bone If a living bone is protected from functional stress osteoporosis may develop The physiological range of forces which cause the bone to follow Wolff s law of adaption to functional demand is not known There is much confusion about the effect of different kinds of load (dynamic or static) on bone Relatively small dynamic pressure changes may engender bone resorption These forces may be developed by a growing aneurysm for instance or by a foreign body anchored to bone undergoing passive movement (Perren et al) The effect of static load is not the same Key and Charnley have shown that osteotomised cancellous bone fixed under static pressure will quickly unite by new bone formation

Little however is known about the reaction of living cortical bone to different amounts of static load and what circumstances lead to a condition such as pressure necrosis (Rustizky) Rigid fixation of necessity depends on inducing areas of pressure* between bone and metal and between bone fragments Since bone and metal have high moduli of elasticity even a small loss of bone due to pressure would instantly eliminate the pressure areas and thus result in loss of rigidity

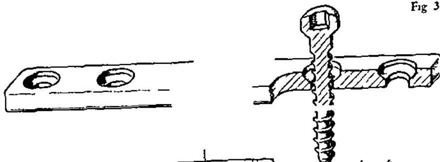
It seemed important therefore to determine how compression might decrease over a long period when a static load was applied to live cortical bone For this purpose a system of load sensitive compression plates has been designed The application of these to normal or osteotomised diaphyseal bone was intended to provide continuous or intermittent pressure recording over a period of several weeks The object of this paper is to describe the construction of this plate the technique of pressure recording and the information obtained from preliminary experiments

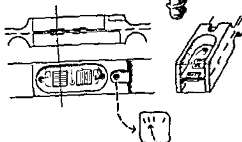
It would have been attractive to use the ferromagnetic device of Willenegger and Straumann with the prospect of real telemetry but this presented difficulties due to tissue reaction to the material and the need to compensate for bending and torque

MATERIAL AND METHOD

As figure 1 shows bone may be put under longitudinal compression by applying an internal fixation plate using a compression clamp (compressor) The amount of the axial compression of the bone is equal to the axial tension in the plate (Fig 2) if weight bearing and muscle contraction are eliminated

* In the sequel we use the words pressure and compression synonymously although strictly speaking the word pressure should be reserved for a state of three dimensional hydrostatic pressure





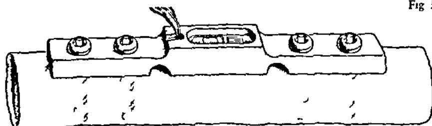


Fig 3—5 A small four hole AO plate is modified (Fig 3) providing it with a strain gauge compartment (Fig 4) to measure longitudinal stress in the plate The plate is fixed to the bone as shown in Fig 5 using the compressor (Fig 1)

1 to permit recording of longitudinal stress in the plate
2 to permit stable internal fixation of two diaphyseal fragments produced by osteotomy or fracture
3 the device must be well tolerated by the tissues

The strain sensitive device in the plate (Fig 4) is constructed using strain gauges which alter their electrical resistance in proportion to forces applied in the long axis of the plate The resistance changes of the strain gauges are measured by a special carrier frequency bridge (Peekel WE 6002 precision bridge or Tepic Indikator IT 1) Metallic foil strain gauges (Frischen MFS FG R = 120 Ohms k = 2) are preferred to semiconductor gauges as the latter are not yet considered sufficiently temperature stable

or ASIF

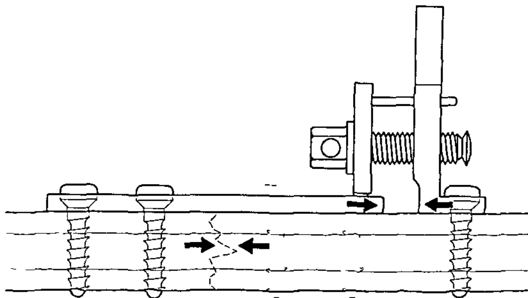


Fig 1 The AO* compressor is used to apply the AO* plate under tension The compressor is removed after driving home the middle screw on the right hand side of the fracture

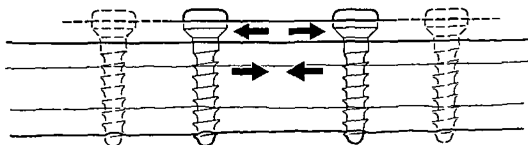


Fig 2 Cortical bone is compressed longitudinally by an internal fixation plate applied under tension The amount of traction in the plate equals the amount of compression of bone if external forces resulting from weight bearing or muscle contraction are avoided

A gauge plate has been constructed It is a modification of the AO* plate as developed by M E Muller (Fig 3) The plate is made of type 316 L stainless steel of which the ultimate tensile strength is about 90 Kp**/mm and the Young s modulus 19 000 Kp **/mm The original AO screw with standard thread and recessed head and made of the same material as the plate is used The holes for the screws in the bone are drilled and tapped and the plate applied with the special compressor (Fig 1) exactly as described by M E Müller Allgower and Willenegger Located between the two middle screw holes of the plate (Figs 5 and 6) is a strain gauge compartment which is made of the same piece of metal as the plate The gauge plate is constructed to satisfy the following requirements

* or ASIF
** Kp = Kilopond = Kilogram force

4 Insulation

Any failure of insulation would shunt the strain gauges Insulation defects may be asymmetrical thus imitating a change of the resistance of the gauge and thereby producing a false reading To avoid such errors the resistance of the gauges versus the plate is measured regularly and plates with insulation defects are discarded

5 Leads

Changes in the resistance of the leads would also imitate changes in the gauge resistance By connecting the strain gauges within the plate to each other to form a Wheatstone bridge the system is much less sensitive to changes in the lead resistance

To test the gauge mounting for possible creep a constant load of 100 Kp was applied to 6 plates and strain recordings were taken during 1 week In one of these plates strain was recorded during 10 weeks

To find out to what extent stress relaxation due to inelastic deformation of the plate or screw would affect the plate on bone system in 2 experiments a gauge plate was applied to a steel tube and an initial load near 100 Kp was installed Strain recordings were then taken during 8 weeks From these recordings an upper bound on the amount of stress relaxation to be expected in the plate on bone system was estimated The estimate was made from a simple model which included in an approximate way the effects of material and geometrical properties of the plate and the material beneath A value for the Young s modulus of a sheep tibia was measured in a simple compression test and found to be 2100 Kp/mm² The calculated rate of elongation of the gauge plate was 1μ/100 Kp On this basis the elastic deformation of bone was estimated to be between 10μ and 20μ depending upon the assumed stress distribution

Before use each plate was tested in a special machine (Fig 8a) The testing procedure included the following steps

1 The relation between measured strain and axial load was plotted over a range from 0—100 Kp (Figs 8a 9 and 10)
2 The influence of temperature was tested in a saline bath at temperatures of 27° 37° and 47° C (Figs 8a and 9)
3 The influence of bending and torque was measured applying a constant moment of 20 cm Kp (Figs 8d 8e and 10)
4 The insulation of the gauges was tested and plates with an insulation resistance <10⁸ Ohms were discarded

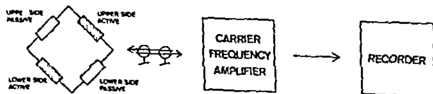


Fig 7 The load cell contains 4 strain gauges forming a Wheatstone bridge which compensates for temperature and bending influences The gauge plate is connected to a carrier frequency amplifier which drives a recorder

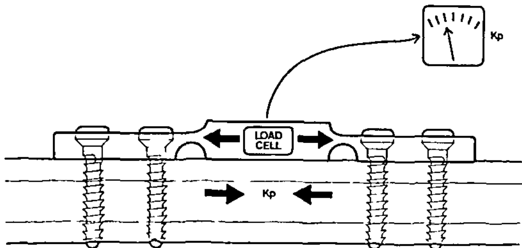


Fig 6 The load cell incorporated in the plate permits continuous recording of longitudinal traction in the plate and thus measurement of compression in the osteotomy

When using strain gauges in such a load cell care must be taken to
1 compensate for temperature changes
2 prevent plastic deformation of the load cell
3 compensate for bending moments
4 ensure good insulation
5 prevent errors due to resistance changes in the electrical leads

1 Temperature

Temperature changes affect the strain readings due to
a) thermal expansion of the underlying metal
b) thermal changes in the resistance of the gauges

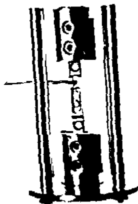
Thermal expansion of the underlying material may be easily compensated for by the use of appropriate gauges Temperature effects on the gauges resistance may be compensated for by the use of twin gauges which are both at the same temperature level but only one of which is under strain In the present system temperature compensation is achieved by the use of a pair of identical gauges one of which is in the long axis of the plate the other at 90⁰ to it

2 Deformation

The relationship between stress and strain is linear only if the metal beneath the gauges is stressed within its own elastic limits To prevent any overload due to bending and torque the chamber is provided with weakend segments to prevent plastic deformation of the load cell (Fig 4)

3 Bending

There remains a possibility of some elastic deformation by bending Two pairs of temperature compensated strain gauges are located equidistant from the neutral axis of bending They are connected to a Wheatstone bridge circuit the balance of which is affected only by axial forces acting on the load cell and not by temperature changes or bending forces This arrangement is simpler to achieve than using one pair of strain gauges placed exactly in the neutral axis of bending (Figs 5—7)



8c

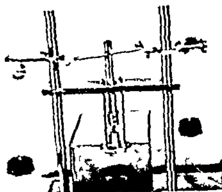


Fig 8d

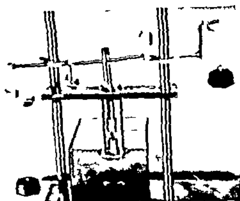


Fig 8e

Fig 8c The gauge plate is mounted with the use of two clamps

Fig 8d Calibration of indicated strain versus torque (20 cm Kp)

Fig 8e Calibration of strain versus bending A constant moment over the whole length of the plate is applied (20 cm Kp)

RESULTS

The curve made by plotting axial force against measured strain is shown in figure 9 In the same figure the error due to temperature changes is also plotted The calibration curve is linear and the influence of temperature is small

The errors due to bending forces in two directions and due to torque are indicated in figure 10 The influence of these forces is negligible

The strain re ording of the plate with a constant load acting demonstrated that the creep of the strain gauge mounting was very small

Fig 8a Test rig shown ready to calibrate indicated strain versus longitudinal traction at different levels of temperature The gauge plate placed in a temperature controlled bath of saline is loaded by the use of a Jack Screw The applied load is measured with a dynamometer (Fig 8b) while the precision bridge at left permits reading of indicated strain

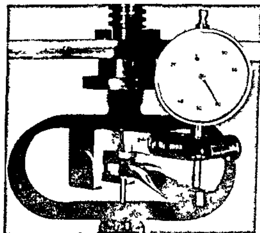


Fig 8b Precision dynamometer to measure longitudinal traction applied to the plate

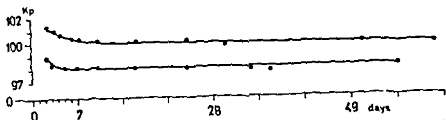


Fig 11 Estimated change of compression in the bone due to inelastic deformation of the plate and the screws

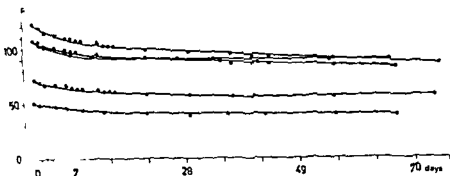


Fig 12 Pressure recording with gauge plates on sterile dead bone at 37° C and high humidity Note the initial fall of pressure due mainly to viscoelastic properties of bone

Figure 11 shows the estimated change of compression in the bone due to inelastic deformation of the plate and screws On the basis of a simplified mo del of the system this deformation was estimated to be less than 0 2μ

Figure 12 shows the decrease of compression in intact dead bone in a tempe rature controlled environment of high humidity Here an initial steep decrease is followed by a very slow de rease The total loss of ompression over 8 weeks is of the order of 20% of the initial value

DISCUSSION

The gauge plate has proved to be useful in recording the change of axial compression of bone In preliminary experiments the strength of the plate and the tissue tolerance were found to be adequate Very little creep has been en c untered in the strain gauge mounting Furthermore the experiment with plates on steel tubes revealed little stress relaxation due to inelastic deformation of the plate and the screws

The experiment using freshly removed tibiae has shown a decrease of the order of 20% which cannot be accounted for by biological processes This de crease occurs in the first few days and is followed by no appreciable long term decrease It most likely results from th viscoelastic properties of bone itself (Sedlin)

Fig 9 Calibration curve plotting applied load versus indicated strain at different temperatures The relation is linear and the temperature influence small The strain is expressed in μm/m

Force acting on the plate	Tension	Bending 20 cm Kp	Bending 20 cm Kp	Torque 20 cm Kp
Indicated strain μm/m	500/100 Kp*	— 1 5 ± 3	+ 4 0 ± 3	— 0 3 ± 4

Fig 10 Indicated strain versus different kinds of forces Mean values and standard *errors of a group of 6 plates are listed*

* each plate is calibrated according to figure 9

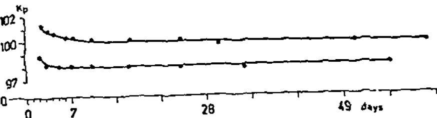


Fig 11 Estimated change of compression in the bone due to inelastic deformation of the plate and the screws

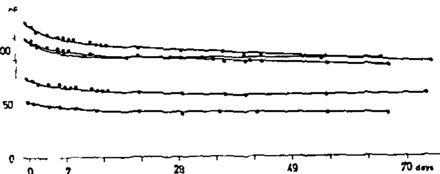


Fig 12 Pressure recording with gauge plates on sterile dead bone at 37° C and high humidity Note the initial fall of pressure due mainly to viscoelastic properties of bone

Figure 11 shows the estimated change of compression in the bone due to inelastic deformation of the plate and screws On the basis of a simplified model of the system this deformation was estimated to be less than 0 2μ

Figure 12 shows the decrease of compression in intact dead bone in a temperature controlled environment of high humidity Here an initial steep decrease is followed by a very slow decrease The total loss of compression over 8 weeks is of the order of 20% of the initial value

DISCUSSION

The gauge plate has proved to be useful in recording the change of axial compression of bone In preliminary experiments the strength of the plate and the tissue tolerance were found to be adequate Very little creep has been encountered in the strain gauge mounting Furthermore the experiment with plates on steel tubes revealed little stress relaxation due to inelastic deformation of the plate and the screws

The experiment using freshly removed tibiae has shown a decrease of the order of 20% which cannot be accounted for by biological processes This decrease occurs in the first few days and is followed by no appreciable long term decrease It most likely results from the viscoelastic properties of bone itself (Sedlin)

Fig 9 Calibration curve plotting applied load versus indicated strain at different temperatures The relation is linear and the temperature influence small The strain is expressed in μm/m

Force acting on the plate	Tension	Bending 20 cm Kp	Bending 20 cm Kp	Torque 20 cm Kp
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FROM THE LABORATORY FOR EXPERIMENTAL SURGERY
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DAVOS SWITZERLAND
(Stephan M Perren head)

THE REACTION OF CORTICAL BONE TO COMPRESSION

by

S M Perren A Huggler M Russenberger M Allgöwer
R Mathys R Schenk H Willenegger and M E Muller

with the technical assistance of V Geret and E Frey

In the «plate on bone» system a total load of 100 Kp results in an elastic deformation of only 10—20 μ Since small changes in the length of the system will result in large changes in force the gauge plate is suitable for measuring the small ch nges in bone length which might be caused by creep resorption or failure of fixation

As a whole the method now seems to be ready for use in living animals Results on the behaviour of intact living bone and osteotomised living bone will be reported below

SUMMARY

The reaction of bone to compression is of primary importance in the internal fixation of fractures Any induction of «pressure necrosis» and consequent bone resorption would result in total loss of rigidity A gauge plate has been developed to study in vivo the reaction of bone to compression by recording the change of load in the bone with time The method permits detection of minute changes in bone length due to creep resorption or instability It is therefore a valuable tool for investigating the quality of a fixation over extended periods of time

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THE REACTION OF CORTICAL BONE TO COMPRESSION

INTRODUCTION

Rigid internal fixation by necessity depends on the production of local pressure areas between implant and bone or between bone ends Wherever pressure necrosis and consequent bone resorption occurs there will be a loss of stability It is vital therefore to understand precisely the reaction of bone to static compression*

Clinical experience shows that bone can withstand a considerable static load without pressure necrosis becoming apparent (Lambotte Danis Lane Hicks M E Muller Allgower and Willenegger) Quantitative information however is lacking about the type and magnitude of forces which will promote functional adaptation of bone structure to stress according to Wolff s law

There are two ways of measuring the change in pressure applied to bone One employs a system with a comparatively high deformability while the other uses a system of very low deformability

— In highly deformable systems the use of ordinary springs permits the determination of load continuously (Burri) or at the beginning and at the end of the experiment (Friedenberg & French) This method cannot detect small amounts of bone resorption as compression depends mainly on the deformability of the spring rather than of the bone Furthermore such a system can become unstable at low pressures

— In systems of low elastic deformability load sensitive metal plates are fixed to the bon Here the deformability is infinitesimal compared with systems using springs These systems thus are able to detect small changes in bone length due to e g creep or resorption

Straumann designed a measuring plate that employed ferromagnetic material and this was used in animals by Willenegger Telemetric readings of tension acting on such a plate were obtained by inserting the limb into a magnetic field Accurate measurements were difficult however because of the effects of torque and bending and precise positioning of the plates in the magnetic field was impossible when using living animals The ferromagnetic materials hitherto available also corroded badly in the tissues

In view of these facts a four hole AO** compression plate of M E Muller s design was modified to incorporate strain gauges and thus to act as a compression plate and load cell at the same time This plate allowed long term pressure recordings to be made unaffe ted by temperature changes and bending stresses The plate itself was well tolerated l y the tissues Its precise specifications have been described above (p 14)

In the sequel we u e the words pressure and compression synonymously although strictly speaking the word pressure should be res rved for a state of three dimensional hydrostatic pressure

** or ASIF

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** or ASIF

It is the purpose of this paper to report the reaction of the living tibial diaphysis of the sheep to known amounts of pressure load comparing the normal to the osteotomised tibia Changes in load are the main demonstration of physical alterations occurring in the bone and are related to the histological appearance

MATERIAL AND METHOD

To apply static compression to the bone four hole plates with built in strain gauges were used as described previously (p 9) The gauge plate compensated for bending moments and temperature variations gave either continuous or intermittent recordings The plates were applied under tension to exert compression as described by M E Müller Allgower and Willenegger

Sheep 2—4 years old were used as experimental animals They were anaesthetised with Fluothane®[1]) (Hutzschenreuter & Perren) The tibia was approached from the medial side preserving the proximal nutrient artery When the tibia had been exposed subperiostally the gauge plate was fixed to the bone The electrical leads were brought through the skin above the femoral trochanter to prevent retrograde infection One of two procedures was then followed

In 6 sheep of group A the plate was applied to the intact bone while in 9 sheep of group B an osteotomy was performed using a very fine saw that cleanly removed 0 1 mm of bone (Willenegger et al) Continuous irrigation with Ringer s solution and slow movements of the saw prevented any thermal damage To prevent splitting of the bone during osteotomy a special bone clamp was used As the operated leg of the animal takes full weight soon after the operation two plates were applied at right angles to each other

At the end of the operation the wounds were irrigated with Polybactrin®) (solution containing Bacitracin Neomycin and Nebacetin) and the skin closed with one layer of 4—0 dermalon®[3]) sutures using Allgower s technique The suture was then protected by Nobecutan®[4]) Spray and no dressing was applied Negative pressure drainage was maintained for 24 hours using a disposable vacuum generator (Protevac®[5]) attached to the animal

The amount of strain placed on the plate was measured while the compressor was being tightened until the required level was reached The first base line reading was taken no sooner than 3 hours after operation to ensure that temperature equilibrium had been reached and the initial stress relaxation of bone had diminished

Pressure readings were taken as described above (p 9) A few animals were followed continuously but in most of them recordings were made at weekly intervals X rays* were taken in a p and lateral projections every three weeks

The sheep were kept as long as measurements were technically possible and were sacrificed only when the leads broke which in group B (osteotomised tibia) occurred between 3 and 12 weeks after operation while in the group A (intact tibia) breakage occurred between 7 and 12 weeks In some animals not listed here measurements after 16 weeks were possible Specimens were removed and embedded in Acrylic after fixation with 40% alcohol and staining with alkaline

* OSRAY® Film Agfa Gevaert AG Basel

[1]) P Geistlich AG Wolhusen
[2]) Pharmacalmic SA Zurich
[3]) Ulrich & Co St Gallen
[4]) Globopharma AG Zurich
[5]) Protek AG Bern
[6]) Opopharma AG Zurich

Fuchsin The bone segments were then cut into thin slices and ground to 50 without decalcification All animals had received 500 mg of Aureomycin®*) intra venously at various intervals after operation and remodelling of the bone could be studied by fluorescent microscopy

It must be emphasized that many preliminary experiments were required to define long term measuring techniques in live animals Difficulties arose from failure of insulation retrograde infections and bending deformations in some early gauge plates Animals with any of these failures are excluded from this report whereas on occasion of broken leads the animals were sacrificed but the results are included

RESULTS

The pressure readings in group A (intact bone) are shown in figure 1 There is a gradual decrease of pressure over 12 weeks after a somewhat steeper decrease in the first few days

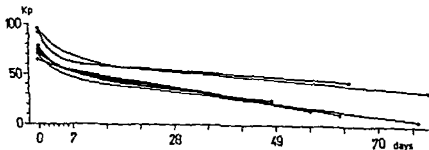


Fig 1 Pressure recording of group A where the plate was applied to intact bone The pressure decreases gradually over 12 weeks after a steeper initial fall

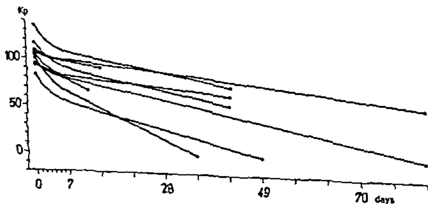


Fig 2 Pressure recording in group B where the tibia was osteotomised The rate of change of pressure is similar with or without osteotomy (fig 1)

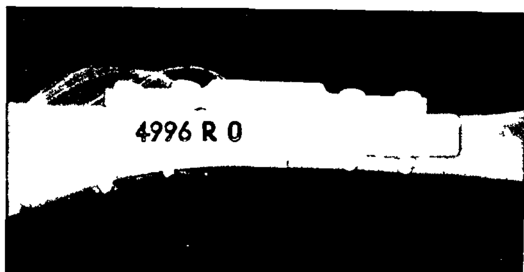


Fig 3 X ray taken immediately after operation The positioning of the two plates placed at right angles may be seen bridging the transverse osteotomy of the tibia

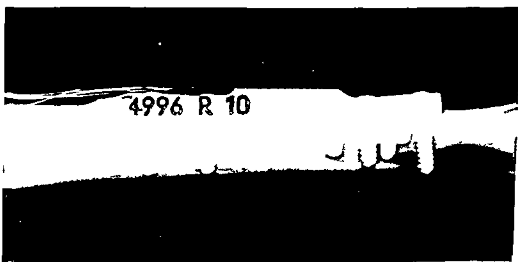


Fig 4 X ray taken at 10 weeks after operation In spite of full weight bearing very little callus can be seen Bony union has occurred

Fig 5 Histology of the cortex beneath the plate 12 weeks after operation Primary fracture healing is seen in spite of full weight bearing No specific resorption of the compressed surfaces is visible



Fig 6 Histology of the opposite side to the plate The gap between the fragments is first filled by lamellar bone (transverse osteon) which in turn will be remodelled later in axial direction Fluorescent label given 3 weeks after operation is found in such a transverse osteon The animal was sacrificed at 12 weeks

The pressure readings in group B (osteotomised bone) are shown in figure 2 The same initial decrease of pressure as in intact bone is seen After this initial decrease the rate of change of pressure is similar to the one in intact bone The rate of decrease of pressure does not depend on the initial level of pressure

Typical radiographs of an osteotomised tibia are shown in figures 3 and 4 In figure 3 the transverse osteotomy of the tibia is seen fixed by two gauge plates A part of the wire connection between the implanted gauge plate and the measuring bridge outside the animal is visible

In figure 4 the radiograph taken 10 weeks after the operation shows the osteotomy gap bridged directly by bone while no external callus is seen in spite of early full weight bearing

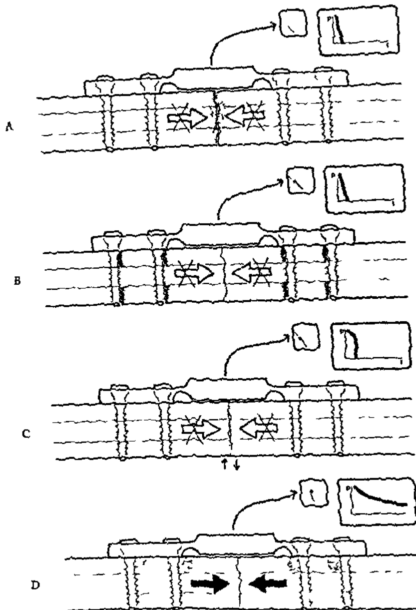
The histology of the specimen removed 12 weeks after osteotomy is shown in figure 5 It confirms the X ray finding of «primary bone healing In no case is there any development of interposed fibrous tissue or cartilage This shows that in spite of full weight bearing the osteotomy is bridged by direct Haversian remodelling It can be seen that in the cortex which is in contact the plate the new bone spanning the osteotomy is formed mainly in the long axis of the tibia In the osteotomy of the cortex opposite to the plate the osteons are first laid down transverse to the long axis of bone but later remodelling takes place in the long axis as in the other cortex The tetracycline label administered three weeks after operation is found in the transverse osteon (Fig 6)

DISCUSSION

After application of compression there is no sudden drop of pressure This statement applies to intact as well as to osteotomised bone under compression of 60—140 Kp The system is sensitive to very small changes in length (a few micra) and the pressure would have decreased to zero if there had been a loss of substance of 10—20μ due to resorption This resorption could occur either at the compressed interfaces of the osteotomy (Fig 7a) or of the screw thread (Fig 7b) Minute changes of length due to instability would also cause sudden changes of pressure (Fig 7c)

The data indicate that at pressure levels of group A (intact bone) and B (osteotomised bone) namely at pressure levels of 60—140 Kp no «pressure necrosis» is present If a layer of bone as thin as 2—3 red cells disappeared at the compressed bone surface a complete loss of compression would result In fact resorption of the compressed interfaces is not even observed at the small area of compressed bone at the screw site where a total pressure of 140 Kp results in a specific pressure exceeding 400 Kp/cm Regardless of the initial pressure there is an identical rate of change

From the results it is reasonable to conclude that rigid fixation was maintained since any movement of the two fragments (even in the range of a few micra) would have resulted in a sudden change of pressure and most probably in a complete loss of compression The fact that the pressure recordings permit conclusions about long term stability of fixation has interesting potentialities in testing new devices for internal fixation (see p 45)



Fi * The effect of various forms of bone resorption and instability on applied pressure in internal fixation

Minute amounts of bone resorption at the compressed bone surface either at the osteotomy (A) or at the screw thread (B) would lead to a steep fall of pressure By a similar mechanism minute amounts of instability (C) would result in a sudden change of pressure Longitudinal resorption of bone (Haversian remodelling) explains the slow and gradual fall of pressure (D) as seen in our experiment (Fig 1 and Fig 2)

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most of the load to the quadrant of bone between the plates and much less to the opposite one

Nevertheless the highest stress of the order of about 400 kp/cm is found at the screw sites and still there is no evidence of pressure necrosis This finding is in line with that of Charnley who found it unlikely that necrosis at a pressure level of 3000 lbs/sq inch (~ 210 kp/cm) would occur

The pressure within the range studied by us leads to a slow loss of load due to Haversian remodelling If Haversian remodelling takes place at any cross sectional area in the compressed segment the pressure will decrease

The data obtained clearly shows that static compression does not neccesarily induce pressure necrosis It seems probable that motion (which may be regarded as being intermittent pressure reaching zero level) does induce bone resorption (Perren et al) which may also be induced by infection The observed slow decrease of compression in the present experiment is due to remodelling

SUMMARY

A new gauge plate was used to study the change of compression applied to intact and osteotomised sheep tibiae No steep fall of compression was seen indicating that there is neither pressure necrosis nor instabili y of fixation A correlation between the slow decrease of pressure and the rate of Haversian remodelling has been established for intact and osteotomised bone In spite of unrestricted weight bearing primary fracture healing was seen

The second observation is the slow but continuous reduction of the pressure in the intact as well as in the osteotomised tibiae When the gauge plates are fixed to a steel tube there is an initial pressure drop which when corrected for bone would be about 2% On dead bone there is a loss of about 20% of the originally applied load (see p 15) occurring mainly in the first week probably due in part to viscoelastic behaviour of the bone (Sedlin) A pressure loss above 20% should therefore be attributed to the response of living bone reacting to load conditions The pressure does in fact fall to 50% within 2 months and the experiments which could be followed over a longer period indicated a further decrease of pressure reaching a new equilibrium near zero in 3—5 months

The similar decrease of pressure in intact as well as in osteotomised bone *indicates that the rate of change of pressure does not depend on any specific* change peculiar to the osteotomy This striking conclusion is based furthermore on the fact that the pressure recordings exclude any movement at the compressed surface of the osteotomy and that the histology (Fig 5) does not show any surface resorption of the compressed area

The histology gives a clue to the decrease in the compression force It shows an intense Haversian remodelling of the compressed tibia In their work on the dog radius Schenk and Willenegger noticed a remodelling rate of 60% *within 8 weeks of osteotomy This seems to be of the same order as that of the* sheep though this animal seems to remodel at a slower rate than the dog The physical effect of this process is the destruction of the osteons under pressure thus reducing the load bearing area of the compressed diaphysis (Fig 7d) The loss of compression is not a linear function of the remodelling rate because the newly formed osteons will be loaded again when further osteons disappear The fact that about 50% of the load has disappeared 2 months after loading would correspond well with Schenk s observation that at this time 60% of the osteons were remodelled

Is living bone able apart from Haversian remodelling to alter its elasticity (as might occur by the direct dissolution of calcium apatite)? This cannot *be answered from our experiment In view of the obvious effect of Haversian* remodelling such a mechanism seems to be neither necessary nor likely

This work shows that a static preload of 60—140 kp on a cortical bone segment about 5 cm in length and between 1 5 and 2 0 cm in diameter does not in*duce rapid pressure necrosis An osteotomy in this segment in vivo does not ap*preciably alter its response to static pressure as long as it is rigidly fixed It is worth noting that «pressure necrosis» at this interface is absent and direct bridging occurs

Two relatively short plates applied at right angles were used in our experiments as immediate weight bearing might have thrown a bending stress on a single plate The disadvantage of too much «stress protection of the plated part of the bone had to be accepted *(Double plating in human* fractures is rarely indicated and only then at the epiphyseal area of long bones) Two plates may prevent the major action of physiological stress and result in bone resorption prevailing over bone formation In our experiment *this effect seems to be partly* offset by the comparative shortness of the plate and by the early weight bearing

Expressing the value of pressure per unit of area is not felt justified as the distribution of load is not uniform Plates applied at right angles *would transmit*

FROM THE LABORATORY FOR EXPERIMENTAL SURGERY
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A DYNAMIC COMPRESSION PLATE

by

S M Perren M Russenberger S Steinemann
M E Muller and M Allgower

with technical assistance of V Geret and M Kiebl

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A DYNAMIC COMPRESSION PLATE

INTRODUCTION

Compression fixation of fractures and osteotomies has gained wide acceptance in recent years Danis was probably the first to design a rigid longitudinal compression system using a plate screwed to the bone cortex and compressed by a device incorporated in the plate Using this technique Danis was successful in securing radiological primary bone healing in fractures of the forearm bones and of the tibia The application of such a plate however is not without its difficulties As no advantage is gained by leaving the compression device in situ M E Müller has devised a separate compressor (see p 8) which can be removed after the plate has been fixed to the bone The use of rigid plates of various sizes combined with the removable compressor has been widely tested by the AO* group and has become known as AO* compression plate technique**

The effect of known values of different static loads on intact as well as osteotomised diaphyseal bone has been thoroughly studied (p 17) A tension force of 60— 140 Kp exerted on a rigid AO* plate will apply a corresponding compression force to the underlying cortical bone It has been shown that under these conditions a resorption of 10—20μ at the interface of an osteotomy or at the screw sites would result in an immediate abolition of the compression force (Perren et al see p 25) No such phenomenon was observed On the contrary well apposed osteotomy surfaces in dogs and sheep united directly by a process of simultaneous resorption and osteogenesis in the axial direction There was however a gradual decrease from the initial load over the course of 3—5 months until a new equilibrium near zero pressure was reached This gradual decrease in compression was matched by the histological finding of longitudinal Haversian remodelling of the cortex The u e of this compression type plate has been evaluated by experimental work on dogs (Schenk and Willenegger Anderson J Muller) and sheep (Perren et al., see page 23) It has also been successfully applied to clinical cases especially for fractures of the forearm and tibia as well as for non unions (Anderson J Muller M E Muller Allgöwer and Willenegger)

The rigid compres ion plate with a separate compressor has some minor limitations

1 after removal of the compressor there is an unpredictable change in the forces exerted by the screws inserted in the coni al holes of the plate Very small displacements of the screw in the plate can result in large pressure changes Such a pressure change will occur if a screw is placed in a conical countersink with even a small amount of eccentricity

* or ASIF

It should be emphasized that compression is not confined to the use of plates nor s compression always appl ed in the long axis of the bone Wherever large and comminuted fractures are bridged by plates compression is first exerted in a plane perpendicular to the fracture by screws crossing this plane

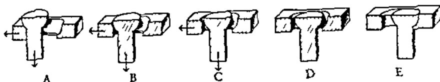


Fig 2A—E The osteotomy or fracture is compressed when the screw is driven home from the position A—C Gliding movement is possible from position D Position A results in a horizontal displacement of 1 5 mm (3 mm total if both sides are used in this position) This position is scarcely ever necessary and will not be discussed further Positions B and C result in less displacement and less compression
Pos tion D final position offers optimum stabil ty with three dimen ional contact
Position E at the end of gliding movement should be avoided

the closure of the fracture During all these movements the screw will be maintained in optimal lateral stability which could not be achieved by pre vious slotted plates

b) the countersunk part of the screw (screw seat) was made spherical to fit the cylindrical shape of the screw hole

c) the Young s modulus of the plate was decreased so that more functional stress could be transmitted to bone According to Wolff s law a more normal bony structure would then result To provide the desired elastic properties and good corrosion resistance of the plate (Hoar and Mears Steinemann) titanium was chosen

Oval compression holes and plates with slots have been used before Eggers devised his sliding plate to prevent deleterious gaps between the fracture sur faces His own studies however using teleradiology showed that the bone ends rarely slid together These plates did not regularly function as hoped because by the absence of a proper countersink fitting between the screw and plate adequate stability was achieved only by eliminating the gliding movement

Bagby modified a Collison plate so that a conical screw head sinking into a screw hole against a straight edge could close an osteotomy gap Tightening the screw automatically pushed the screw towards the fracture or osteotomy resulting in adaption of the bony surfaces He concluded that wherever good contact of osteotomised surfaces was present together with rigid fixation union occurred regardless of the amount of compression present However he rightly pointed out that compression increases stability In the present work a shape of screw hole was developed which retains the desirable compression and in addi tion offers the optimal lateral stability that was considered to be improvable in Bagby s design

Oblique screws do not achieve similar compression since once the plate is in contact with bone seating an oblique screw will not result in any displacement of the plate relative to the bone

The new plate which is described in detail on page 32 offers definite advan tages over the well tested AO* plate provided that rigidity is maintained This is synonymous with maintenance of applied load

The purpose of the present paper is to outline the construction of and to report results obtained with titanium plates similar to those mentioned above These plates were modified by fitting them with strain gauges to measure com pression forces in the osteotomy and thus to monitor the stability of fixation

* or ASIF

2 the removal of stress influences the bone beneath a rigid plate and can l
to some osteoporosis in the cortical bone This has been observed in pla
femora and tibiae especially when two and/or massive plates were used W
such plates are removed fatigue fractures may occur through the porotic a
3 applying a separate compressor requires a wider exposure which may
difficult at some sites
4 the close conical fit between screw neck and plate countersink holds
screw at right angles to the plate This may make it difficult to place
screw in exactly the right relation to a fracture line
5 there may be significant corrosion of *AISI 316 L steel at the screw s*
especially when movements occur (Steinemann) This applies for examp
to the tibia were considerable amounts of stress are transmitted from the scre
to the plate under weight bearing conditions

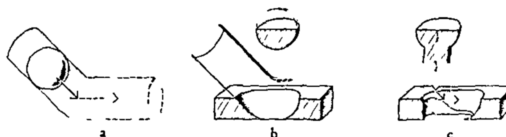


Fig 1a—c The new screw hole which permits compression of the osteotomy (or fra
ture) when the screw is driven home offers adequate stability and prevents any locki
effect
Fig 1a shows how a ball (screw) is guided in a sloped cylinder (screw hole) Any mov
ment downward will result in a horizontal displacement No sideways movement is pos
ble The position aimed at is the intersection of the two cylinders This position offe
best stability without any locking effect In the horizontal cylinder displacement t
wards the osteotomy is possible
Fig 1b Projection of the cylinders into the screw hole and the ball shaped screw
Fig 1c Actual shape of the hole with the slot necessary for the screw neck and thread

It seemed desirable therefore to design a plate providing the same stabilit
across an osteotomy or fracture as the rigid compression plate but avoiding th
disadvantages listed above Three alterations seemed essential

a) the original conical screw hole (see p 8) was altered to a shape which is par
of the geometrical figure formed by two cylinders intersecting an obtus
angle (Fig 1) a sloped one and one in the long axis of the plate (Figs 1a an
b) The screw entering this hole will first be guided by the sloping cylinde
(Fig 1c) A movement of the underlying bone towards the other fragmen
will result (Figs 2A—D) The effect will be first to close and then to com
press the fracture (see also page 48) This eliminates the need for an externa
compressor with the consequent need for additional surgical exposure ir
many cases (e g in undisplaced fractures) This design does not prevent the
use of an external compressor if such a procedure should be desirable (e g in
hip surgery)
The horizontal cylinder will furthermore allow the screw to move a little
further towards the fracture This is to prevent any tendency to obstruct

MATERIAL AND METHOD

The gauge plate used in these experiments was similar to the one used above (see page 9) except for the following modifications

1) the metal used for the plates was commercially pure titanium of which the ultimate tensile strength is about 80 Kp/mm and the Young s modulus is 11 000 Kp/mm The dimensions of the plate were adjusted to compensate for the somewhat smaller ultimate tensile strength of the material

2) the load cell was similar with respect to mechanical and electrical construc tion and the plate was designed to prevent any deformation of the load cell due to bending forces The gauge compartment was arranged to leave a gap of 1 mm between the bone and the bottom surface of the compartment thus allowing tissue to grow between the bone and the plate (Fig 4)

3) the plate has 4—6 sloping cylindrical holes so that when the screws are driven home they exert a compression force on the bone in an axial direc tion (Figs 1—2) The angle of slope was chosen to eleminate any loosening of the screw due to mechanical reasons The screw is spherically countersunk exactly fitting the screw hole Thus the screws have at least a semicircular line of contact with the screw in any position (Figs 3 II & III) At the end of the slope when the screw has been fully driven home an area of contact bet ween the screw and the hole is present amounting to part of the sphere (Fig 3D) This position which offers maximum long term stability should be achieved whenever placing a screw To permit simultaneous adaption and compression of an osteotomy or fracture the sloping cylinder provides a ma ximum horizontal displacement of 1 5 mm (Figs 2A—D) The horizontal cylinder of the screw hole permits an additional horizontal movement of the order of 2 0 mm (Figs 2 D and F)

To position the screw in the hole of the DCP (dynamic compression plate) two different drill guides are used The load guide (Fig 5) places the screw in the slope as seen in figure 3 B When driven home the head slides down the slope displacing the underlying bone towards the osteotomy When the fracture or osteotomy gap has been closed and only slight further compression is needed the neutral guide is used to place the screw near its final position on the slope (Fig 3 C) When the screw is driven home from this position it exerts additional mild compression In practice the neutral guide will be used to position most of the screws and it is vital that on each side of an osteotomy or fracture at least 2 screws are fully driven home

The experimental animals used were sheep from 2—4 years of age Anaesthesia and surgery followed the procedure described above (p 20) with these excep tions

To obtain well standardised experimental conditions for the fixation of the osteotomy a special drill guide was used to drill 2 holes en each side of the osteotomy The drill guide was U shaped and when fixed to the bone prevented splitting during osteotomy As above 2 plates were used to obtain enough stability for safe weight bearing First the four hole plate was applied on the posterior aspect and then a six hole plate was fixed on the medial aspect of the tibia in a similar manner this latter plate giving about 20% higher compres

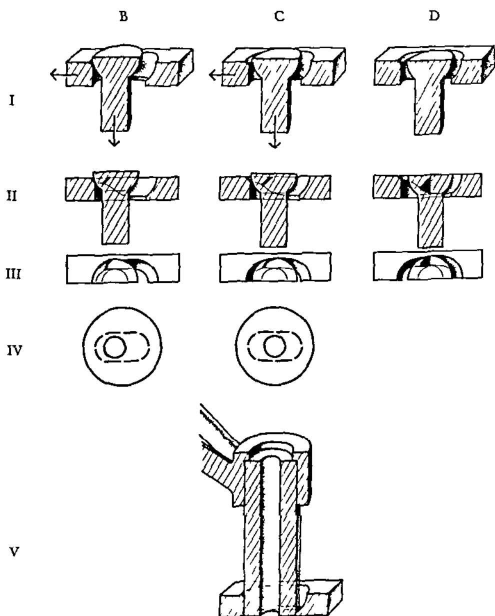


Fig 3 B—D Relation of screw head and screw hole and positioning of drill guides
B Positioning of the screw by the load guide (dislocates the bone fragment approximately 1 mm when the screw is driven home)
C Positioning of the screw by the neutral guide Screw is placed near the end of the slope so that very little dislocational force results Compression instituted by the load guide» is slightly increased
D Position of screw when fully driven home

I Longitudinal section through screw and plate
II Line of contact between screw and hole seen from side
III Line of contact between screw and hole seen from above
Note Semicircular line of contact in B and C while in D the area of contact is part of sphere
IV Cross section of the corresponding positions of the drill guides
B Load guide
C Neutral guide
V Longitudinal section of the drill guide placed in a screw hole

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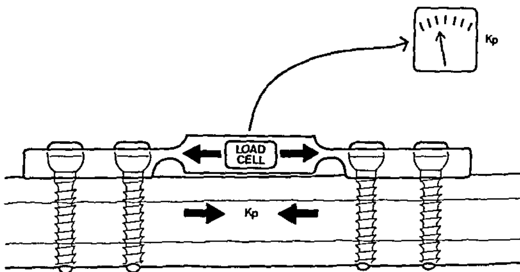


Fig 4 Gauge plate used to control stability of fixation achieved by the dynamic compression plate The slightest movement of the fragments due to instability results in a sudden pressure change No such changes were recorded with the dynamic compression plate when used correctly

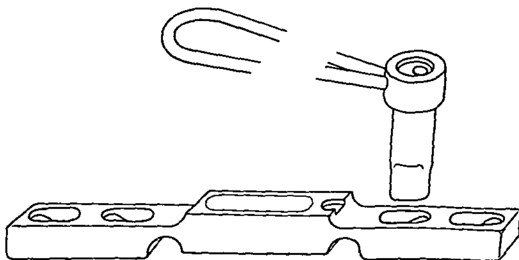


Fig 5 Gauge plate and drill guide Two types of drill guides permit the achievement of compression at two different levels The load guide with an eccentrically placed hole is used as shown in Fig 3 IV B Driving home the screw then results in high compression The neutral guide with the hole in the middle is used to achieve mild compression Fig 3 IV C This guide should be generally used under the condition that good adaption is obtained before

sion than the four hole plate To delay weight bearing until 3 weeks a simple tenotomy of the Achilles tendon was performed

The plates used in animal experiments to be reported here were DCP s provided with strain gauges in a similar manner as outlined for the AO* compression plate (see p 9) The DCP gauge plate is shown in figures 4 and 5 An additional simple metal clamp was employed near the plate to prevent the leads from breaking Thus at the end of the experiment a final reading could be taken even after a lead break by exposing the wire where it had been protected by the clamp In this way a recalibration also could be made after removal of the plate

The above mentioned experiment was performed on 8 sheep An additional group of experiments was done with 4 sheep In this group the osteotomies were performed on the metatarsus using a single plate for fixation and weight bearing was prevented by combining ankle arthrodesis with tenotomy 3 weeks before the osteotomy These animals were observed for 16 weeks An additional animal with a tibia osteotomy fixed by two DCP gauge plates wes observed during 16 weeks In this animal weight bearing was not delayed by tenotomy The specimens of bone were sectioned as described above (see p 20)

RESULTS

The pressure recordings of 8 consecutive experiments which lasted two months are shown in figure 6 The pressure initially applied ranged from 70—180 Kp As with the conventional steel plate the pressure decreased progressively after an initial somewhat steeper drop In those animals which were observed during 4 months pressure gradually decreased before it approached zero with no sudden drop at any point

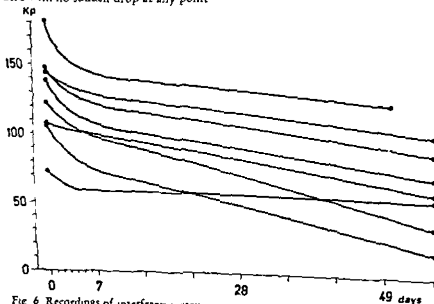


Fig 6 Recordings of interfragmentary pressure in a group of transverse tibia osteotomies fixed by dynamic compression plates There is no sudden fall of pressure

* or ASIF

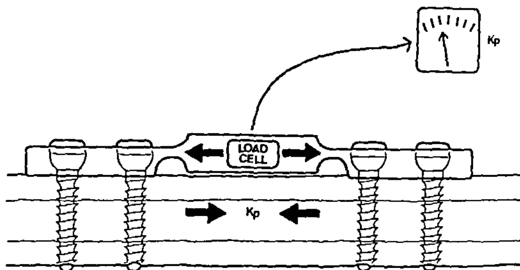


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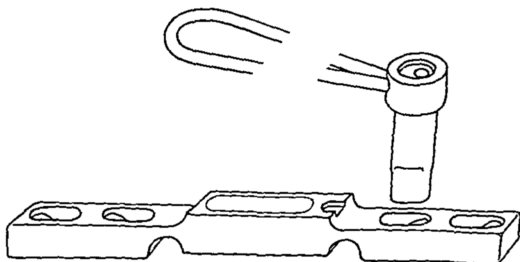


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screw seat did not offer optimum lateral stability This latter problem has plagued most other slotted plates The key to success is congruity between screw and plate which in the present plate is produced by three dimensional seating of a spherically countersunk screw head in a cylindrically countersunk plate This design overcomes the chief disadvantage of the ordinary slotted plates while keeping its primary asset of preventing the plate from holding the fracture gap open

Measurements with DCP s (dynamic compression plates) provided with strain gauges (DCP gauge plates) showed that with the DCP axial compression of the same order as with AO* compression plates with external compressor was obtained Before use in humans it was advantageous to determine wheter the DCP could be relied upon to maintain rigidity as long as the original AO compression plate It was demonstrated that with two DCP gauge plates applied to an osteotomised sheep tibia the rate of decrease of compression measured over 8 weeks matched that obtained with the AO plate (p 21) Experiments with osteotomised metatarsi of sheep stabilised by DCP gauge plates showed a slow decay of pressure over 8 weeks with demonstrable compression forces up to 4 months At no time did a sudden drop of pressure indicate the presence of instability

The histological findings of Haversian remodelling directly bridging the osteotomy without formation of external callus were identical to those observed with conventional steel plates At 8 weeks the osteotomy wa bridged by some osteons but remodelling of the cortex was only partial (Fig 8) At 16 weeks examination of the metatarsi and of the tibia showed the osteotomy to be clinically united with minimal callus formation (Fig 9) The cortex was undergoing extensive Haversian remodelling with much osteogenesis within the canals The DCP clearly fulfil the function of giving sufficient rigidity to allow primary healing

The main function of the horizontal cylinder is to allow for minor d placements of the screws relative to the long axis of the plate The present design of the screw hole permits a screw which has been positioned at the intersection of the two cylinders to move only towards the fracture gap The major reason for allowing this kind of displacement s to prevent screws from locking during the procedure of closing the fracture gap (this procedure may involve several adjustments of the screws in order to ensure optimum fixation) An additional advantage of the allowed axial displa ement is to prevent an eventual imperfect closure from being held apart This type of design also results in a more beneficial stress distribution in pre ious experiments with AO gauge plates we have observed changes of the initially applied pressure when seating subsequent screws In practise the DCP served the above mentioned function while maintaining a sati factory amount of compression and stability

The screw has a spherical seat This shape of the screw countersink allows flexibility in directing the line of action of the screws to achieve the de ired force on the fracture surfaces It also permits to obtain a better grip in comminute fractures

Corrosion and fatigue fractures in compression plates usually occurred in the outer screw holes or at some other highly stressed point of a plate applied to a

* or ASIF



Fig 7 Close up view of a metatarsus 16 weeks after transverse osteotomy and internal fixation with DCP gauge plate The osteotomy is scarcely visible There is minimal callus formation and no periosteal reaction can be detected

Radiographic and macroscopic examinations both showed the absence of exter nal callus formation (Fig 7) The titanium plate provoked no visible reaction in the tissue and in every case a thin sheet of vascular tissue was found to be lying in contact with the metal The bone adjacent to the plate was well vas cularised No titanium dissollution products were observed in the tissue although metal deposits sometimes are seen in human cases

Histology revealed that the osteotomy was directly bridged by new osteons in the pressure area (Fig 9) Beside this area of contact and pressure near the pla tes there was usually a gap between the fragments on the opposite side of the osteotomy Where there was a gap the osteotomised bone clearly did not sup port any pressure Nevertheless such a gap area benefitted from the stability provided by the area which was in contact and supported pressure Under such stable conditions *small* gaps were directly bridged by new osteons (*Fig 8*) *while* larger gaps were first filled with lamellar bone and then remodelled in the long axis of bone (see p 23 Fig 6)

At 8 weeks remodelling was still incomplete (Fig 8) at 16 weeks the osteotomy was healed (Fig 9) There was no significant resorption of the osteotomy sur face seen either at the pressure side» or at the «gap side and in no case was any cartilage or fibrous tissue detected in the gap As seen in figure 9 there was minimal callus present in spite of early full weight bearing in the tibia osteo tomy which was observed for 16 weeks

DISCUSSION

As Egger claimed the function of an implant in internal fixation is to coun teract the forces producing shear or distraction His plate was considered to have failed to achieve this result however since it did not apply compression *to counter* distraction and did not fully prevent shear since the shape of its

* distraction is a movement which results in opening the fracture gap

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In our series of experiments with sheep good rigidity was maintained and prompt healing achieved in two types of experimental osteotomies Based on these results a clinical testing program has been initiated Preliminary results are reported in a separate paper (Allgower et al see p 45)

SUMMARY

Rigid fixation by conventional compression techniques while permitting economical primary bone healing is liable to protect bone from physiological stresses and may thus induce osteoporosis of the cortex Furthermore there is a locking action of a screw hole with conical fitting under weight bearing conditions

A compression plate was constructed therefore which would provide the same amount of stability but prevent locking action of the screws and permit axial compression without the use of an external compressor

Long term pressure recording as well as histology give evidence of maintained stability

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Fig 8 Histology of a transverse tibia osteotomy 8 weeks after fixation with two DCP gauge plates At this time the osteotomy is only partially remodelled The gap at this particular site of the osteotomy measures about 20μ



Fig 9 Histology of a transverse tibia osteotomy 16 weeks after stable internal fixation with two DCP gauge plates remodelling is far advanced At this site of firm contact pressure is transmitted yet there is no sign of surface resorption Note the minimal amount of callus at the end of the osteotomy indicating complete stability in spite of early weight bearing

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INTRODUCTION

Three groups of experimental findings are relevant to the clinical application of compression plates and to possible improvements in their design

Static loads of the order of 60 to 140 Kp applied to cortical bone are found to be maintained over several months and during this time gradually diminish to near zero pressure There is no sudden loss of pressure due to bone necrosis From an engineering standpoint such a compression system therefore is able to secure maximum stability of internal fixation Biologically it is compatible with the healing process The gradual pressure loss mentioned above is induced by bone remodelling of the Haversian system slowly replacing the compressed osteons by new ones There is no appreciable difference in remodelling of a cortex whether an osteotomy is present or not provided the contact surface is rigidly stabilized Remodelling however leads to bridging of the osteotomy gap resulting in direct repair (Perren et al see p 23)

Such a process has been found in the osteotomised radius in the dog (Schenk et al) in the tibia of the sheep (Perren et al see p 24) and in the tibia of the rabbit (Rahn et al) It has also been observed in the tibia of a human adult who died three months after internal fixation

Endosteal or periosteal contribution to bone remodelling consists mainly of increased blood supply to the cortex To what extent endosteal or periosteal callus formation occurs depends on the stability of the internal fixation (Hutzschenreuter et al) The rationale of the rigid AO* compression system therefore is well documented and the high success rate after adequate operation is not surprising (Anderson Rhinelander M E. Muller Allgöwer & Willenegger)

The rigid connection between screws anchored in the comparatively deformable bone on the one side and in the rigid plate on the other has however certain drawbacks

— under weight bearing conditions a rigidly plated bone undergoes a smaller elastic deformation than a bone without plate This difference is the greater the longer the plate A screw head at the end of a 15 cm plate will have a tendency to move towards the center of the plate over a distan e of about 30μ when weight bearing with 100 Kp is instituted This gives rise to considerable stress at the point of contact between screw and plate and may induce corrosion and even fatigue fracture of the screw

— in the conventional procedure using the separate compressor compression is instituted at the beginning of the procedure and then the screws are inserted into the plate Eccentricity in positioning of conically seated screws in such a plate will result in unpredictable alterations in the applied load and in stress concentrations

— elastic deformation of the cortex will be reduced by the locking effect of the tightly fitting screws because the complex of bone and plate will become very rigid The rigidly fixed plate with its high Young s modulus results in considerable stress protection to the plated part of the diaphysis

* or ASIF

especially when double plates are used This — according to Wolff s law of adaptation to functional demand — will cause bone destruction to prevail over osteogenesis in the course of remodelling and thus lead to osteoporosis of the cortex In turn this may give rise to fatigue fracture after removal of the implant

The locking effect of the screws as well as part of the stress protection can be eliminated by a slotted configuration of the screw holes and an increase in deformability of the plate provided that the relative shape of the screw seat is able to protect the fracture from shear and distraction Together with Perren and Russenberger we have been able to design a screw seat which enables a tension force to be applied to the plate by the screw head when the screw is driven home (Perren et al see p 32) The Dynamic Compression Plate (DCP) has been described previously The DCP has been proved to offer adequate stability of fixation Its main specification will be given under material and method It is the purpose of this paper to report our observations in a consecutive series of clinical cases using the DCP Apart from eliminating in most of our cases the necessity for any compression device (thus allowing a shorter incision) this plate seems to offer definite biomechanical as well as metallurgical advantages over the conventional plates made of AISI 316 L as described previously (M E Muller Allgower & Willenegger)

MATERIAL AND METHOD

The dynamic compression plate is made of commercially pure titanium treated to increase the ultimate tensile strength The Young s modulus of titanium (11000 kp/mm) is markedly lower than that of stainless steel or of vitallium® The fatigue resistance of titanium is good (Steinemann) and its resistance to corrosion in body fluid is excellent (Hoar & Mears Steinemann) as in this fluid titanium does not show any pitting corrosion

The over all shape of the plate as seen in figure 1 corresponds to that of the AO* plate The cross section of the dynamic compression plate is slightly larger than of the AO* plate This is to allow for the somewhat smaller ultimate tensile strength of titanium (80 kp/mm) when compared to AO* steel (90 kp/mm)

The screw seat has been designed as illustrated in figures 2 and 3 in order to combine

- compression of the fracture when the screw is driven home
- firm precision fit of the screw head in the screw hole at all times
- prevention of locking effect of the screw

The screw hole the shape of which has been described in detail (Perren et al see p 32) is part of the geometrical figure formed by two cylinders a sloping one and a horizontal one intersecting at an obtuse angle The screw has a spherically countersunk head exactly fitting the cylinders of the screw hole The line of contact between screw and screw hole is a semicircular line At the intersection of the two hemi-cylinders the contact area is part of a sphere In all other aspects the screw is identical with the AO* screw It is not selftapping and has a hexagonal imbus The screw holes of the plate ends will also accomodate cancellous screws with a larger thread

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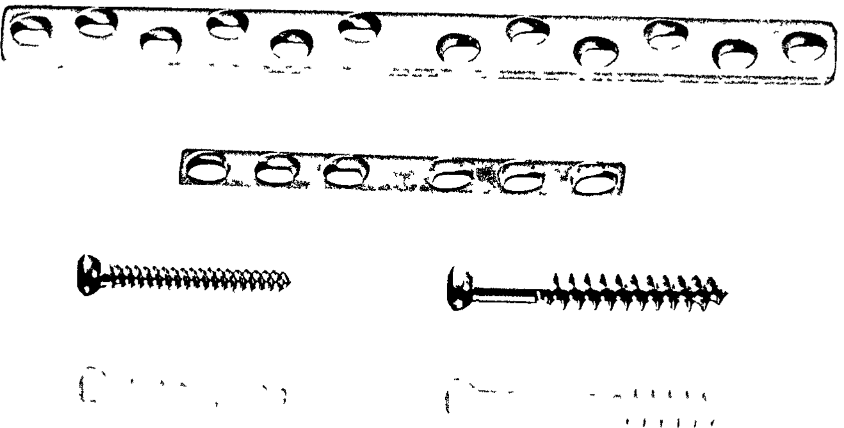


Fig 1 Large and small dynamic compression plate» DCP with cortical and cancellous screws (photograph and section) made of commercially pure titanium Apart from the configuration of the screw holes and screw heads the plates are similar to the conventional plates made of AISI 316 L steel described by M E Muller Allgower and Willenegger

To position the screw in the screw hole drill guides are used (Fig 4) Two different types of drill guide (Fig 5) place the screw either in the middle of the sloping cylinder (load guide A) or near its lower end (neutral guide B) The use of the load guide produces a horizontal displacement of the fragments toward the fracture of about 1 mm when the screw is driven home This guide is used to eliminate the fracture gap The neutral guide is used when the fracture gap has been closed and put under pressure so that only slight further compression is needed

When the screw is driven home there remains the possibility of a passive movement of about 2 mm of the screw head towards the end of the horizontal hemicylindrical screw hole This should prevent any locking effect of the screw to avoid unpredictable loss of load when additional screws are inserted and to reduce the load of each screw Thus axial stress will be transmitted to the cortex when weight bearing is begun or muscular forces begin to act on bones such as those of the upper limb

Up to now 300 human cases have been operated using the DCP with very gratifying results In this first report we only include the first 60 consecutive cases done between January 1966 and February 1967 which until now have been fully followed up namely

- — tibia 53 fresh fractures (two cases of non union and one refracture)
- — radius 2 shaft fractures
- — femur 4 fresh fractures one infected non union
- — clavicle 1 non union

Three patients died from coronary occlusion or pulmonary embolism in the weeks following their injury and therefore are not included in this report although bone healing proceeded normally

There remained 50 tibial fractures in 49 patients who could all be followed up fully They constitute the main part of this report They were contacted 6—8 months after operation by a questionnaire and one year after operation there was an individual examination of each patient After a mean time of 69 weeks (from 45 to 100 weeks) all implants were removed according to the following procedure

1 Distal part of scar opened so that the distal three screws could be exposed
2 Removal of overlying tissue for histological examination
3 Color photograph of plate in situ
4 Removal of all other screws by small incisions and removal of the plate
5 Photograph of plate bed
6 Biopsy of plate bed for metallurgical and histological examination



Fig 2a



Fig 2b



Fig 2c

Fig 2 **Compression fixation by the DCP** Compression is obtained by the spherical gliding principle« The spherically countersunk screw head is congruent to the hemicylindrical sloped screw hole and approximates the bone ends when driven home At the end of the slope the hemispherical screw head has a larger contact area with the plate corresponding to part of a sphere (see also Perren et al Fig 1 p 32) The screw head in figure 2c lies at the beginning of the horizontal hemicylinder of the screw hole which offer the possibility of «pa si e movement of the screw

To position the screw in the screw hole drill guides are used (Fig 4) Two different types of drill guide (Fig 5) place the screw either in the middle of the sloping cylinder (load guide A) or near its lower end (neutral guide B) The use of the load guide produces a horizontal displacement of the fragments toward the fracture of about 1 mm when the screw is driven home This guide is used to eliminate the fracture gap The neutral guide is used when the fracture gap has been closed and put under pressure so that only slight further compression is needed

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Fig 3 Longitudinal section through screw hole and screw head of the DCP
The spherical countersunk screw head is any position congruent to the hemicylinders of which the screw hole consists

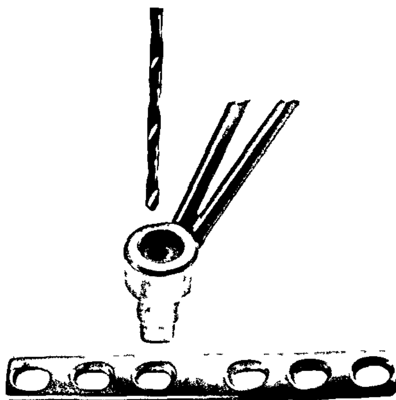


Fig 4 DCP with drill guide and drill
The drill guide fits exactly in the screw hole and thus precisely positions the drill in respect to the sloped cylinder

RESULTS

Tibial fractures (50 fractures in 49 patients)

The average hospital stay was 11 days No infection occurred Two patients showed local tenderness on premature weight bearing which immediately subsided when weight bearing was discontinued No secondary operation was required except for the removal of the plate

During the course of healing there was little discomfort in the operated leg except for the cases mentioned above On removal of the metal 65% considered themselves completely normal 35 % had minor complaints Ankle and subtalar joints recovered completely

All 50 fractures showed good radiological consolidation at the time of removal of the metal (Figs 6c and d) The cortical bone appeared quite homogeneous and dense even deep to the plate There seemed to be more evidence of endosteal callus formation than in cases plated with conventional AO* plates but the difference seems hardly significant The rate of so called primary bone healing which means healing with no radiological evidence of callus was 50 % in this series compared to 70% in previous series with conventional AO* plates

In 37 fractures we were able to remove all implants ourselves In each case the tis ue immediately deep to the plate was macroscopically well vascularized The other tissues surrounding the plate showed in most cases a firm contact with the implant so when removing the plate a thin layer of vascularized tissue adhered to the titanium implant Of 37 fractures 18 showed no evidence of metal deposits whatsoever while 17 had a slight coloration of the tissue surrounding the distal part of the plate located especially at the neck of the screws According to Steinemann such a coloration corresponds to about 100 PPM of titanium in the tissue Two cases showed significant metallic coloration of the tissue It was interesting that visible metal deposits were not parallelled by clinical signs of irritation

Histological examination of the tissue surrounding the plate revealed a comparatively small layer of fibrous tissue adjacent to plate (Fig 7a) Capillaries were seen in the immediate neighbourhood of the implant (Fig 7b) According to the macroscopic findings in about half of the cases metal deposits were seen the quantity of which ranged from detectable to significant deposition (Fig 7c) Histologically titanium deposits hardly provoked any inflammatory reaction or proliferation This finding is consis ent with other experimental findings (Steinemann et al)

Of special interest was the fact that the slotted holes of these DCP s were filled with bone The removal of the plate may thus be somewhat more difficult than with ordinary stainless steel plates Such a bone formation certainly indicates the good tolerance of the metal employed

Forearm fractures and non unions

Both our radii united without any immobilisation of the injured forearm and without any discomfort to the patient (Figs 9 and 10) Figure 11 shows a recent

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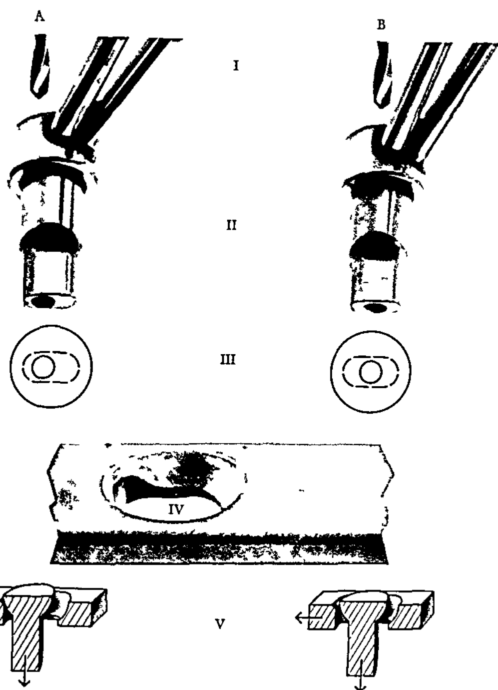


Fig 5 The use of the two different guides (A load guide B neutral guide)
I Drill of 3 2 mm diameter
II Drill guide seen from below (Note the eccentrical hole in the load guide (A) placing the screw on the slope of the screw hole The neutral guide (B) places the screw near the end of the slope thus increasing compression to some extent when the screw is driven home)
III Cross section through the drill guide A) load guide with eccentrical hole B) neutral guide with centrical hole
IV Screw hole of the plate seen from above The drill guide fits precisely in the lower opening of the screw hole
V Dislocational effects of the screw when driven home

case not included in the above mentioned series of a non union of the forearm healing rapidly after fixation by DCP s

The rather avascular non union of the clavicle (Fig 8a) was treated by compression fixation alone without any cancellous bone graft At 50 weeks it showed good consolidation (Fig 8b) permitting removal of the metal at this time

The infected non union of the femur constituted a major challenge because of extensive cortical necrosis and bone defect which had to be replaced by cancellous bone grafts For stabilization a double plate was required and despite the rather massive implant bony union was surprisingly rapid and wound discharge was soon minimal It subsided 6 months before removal of the plates This is a most unusual observation when using other material in infected sites Bone healing in the face of infection may occur with various metallic plates but usually drainage continues as long as the implant is in place In a subsequent series not reported here we had a similar experience with other infected non unions of the femur where the wound also healed promptly

DISCUSSION

The rigid AO* compression plate of stainless steel facilitates the main aims in the operative treatment of fractures and non unions namely full functional recovery combining four principles

— anatomical reduction
— atraumatic technique
— stable fixation
— immediate postoperative mobilisation without externel fixation

The stability achieved is sufficient to neutralize the fracture or the non union allowing cortical bone healing together with immediate postoperative mobilization of the injured limb The drawbacks of the system are marked stress protection of the plated cortex by the locking action of the tightly fitting s rews and unpredictable changes of compression by screws inserted eccentrically

The question arises whether it is possible to avoid the disadvantages of the rigid compression plate without losing its advantages namely the successful neutralization and compression of the fracture

In osteotomised tibiae of the sheep fixed with DCPs we have indeed been able to show that the rate of pressure fall is id ntical to that observed with conventional AO* plates (Perren et al see p 21) This is good evidence that stability is in fact well mainained Results in the clinical series confirm this point very well Not one failure due to instability was encountered in the 60 cases

The next question is whether we have really eliminated the above mentioned drawbacks of the rigid compression plates There are some indications that this is indeed true Cortical bone in the plated area seems more solid and more homogenous radiologically when using DCP than with ordinary AO* plates On removal of the plate the site appears to be distinctly better vascularized The patients also complain less of discomfort in the lower leg fractures but this point evidently is very difficult to quantitate

* or ASIF

Fig 6a

Fig 6b

Figs 6a and b Fracture of both tibiae and fibulae in a 22 year old woman after accident

Fig 6c

Fig 6d

Figs 6c and d Fracture of both tibiae and fibulae in the same patient 80 weeks after application of DCP Note the dense structure of bone underlying the DCP

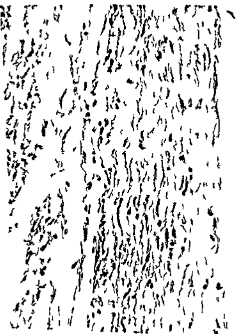


Fig 7a

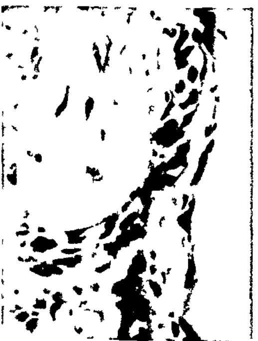


Fig 7b



Fig 7c

Fig 7 Histology of tissue adjacent to the plate
a) Loose connective tissue immediately adjacent to the plate which shows no detectable proliferation or inflammatory reaction
b) Capillary immediately adjacent to the plate
c) Deposit of titanium in tissue at removal of implant (56 weeks after internal fixation)
Absence of inflammatory reaction around metallic deposit Since using anodically oxidized titanium plates no further metal deposits have been observed

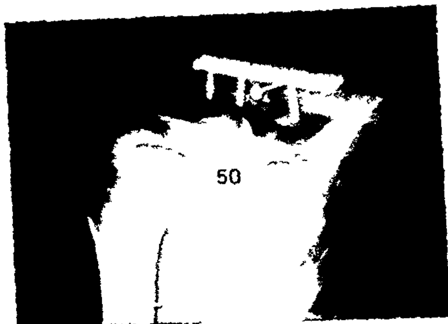


Fig 8b



Fig 8a

Figs 8 a and b Non union of collar bone 18 months after fracture the non union was treated by a DCP and one additional la_g screw (Fig 8a) without any additional cancellous bone transplant The x ray taken at 50 weeks after operation (Fig 8b) shows bony union

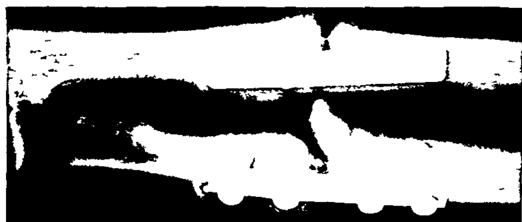
Fig 9a Transverse radius fracture fixed by a six hole DCP and treated without any external fixation showing full functional recovery one month after operation

Fig 9b Result after 62 weeks

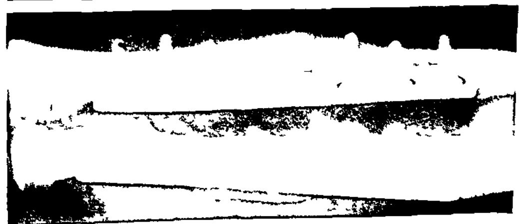
Fig 10a Transverse radius fracture fixed by a six hole DCP and traeted without any external fixation showing full functional recovery one month after operation

Fig 10b Result after 70 weeks

Since we are introducing two changes simultaneously — configuration of the screw hole and change of metal — we are not quite sure which has played the greater role in this respect Titanium however seems to be surprisingly well *tolerated and the increased deformability of the DCP certainly did not com promise the results*







Figs 11 a c a) Non union after inadequate fixation of a forearm fracture
b) X rays taken after 1¹/ months
c) X rays taken after 8 months showing bony union almost completed

Pitting corrosion is no problem with titanium The metal deposits present in about half the cases of this series stemmed probably from pickling The had apparently little clinical signifiance and did not induce tissue reaction (Figs 7a—c) Using anodically oxidized titanium plates we have not observed metal deposits in a further clinical series of 300 cases not reported here

It is well known that Eggers as well as Bagby advocated the use of slotted plates An internal fixation achieved by the use of the Eggers plate does not resist distraction nor shear The lateral support of Bagbys plate was not con sidered to be optimal From our previous observations in the experimental ani mals and now in clinical cases we may conclude that it is possible to use self compressing plates if care is taken that lateral stability and axial compression are as well maintained as with a conventional compression plate This plate (DCP) combining the practical benefit of requiring less exposure with a more physiological stress transmission to the bone cortex therefore may offer some distinct advantages

SUMMARY

The dynamic compression plate (DCP) has been succesfully applied in fresh fractures as well as in infected and non infected non unions Detailed instruc tions for its application are given The DCP is well tolerated by the tissue and offers advantage of less exposure and more adaptability to the individual case The experimental prove of continuous stability as reported in an earlier paper is born out by clinical experience

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MYOELECTRIC SIGNALS IN CONTROL OF PROSTHESES

Studies on arm amputees and normal individuals

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CONTENTS

From the Swedish

by

Lois Goldie Carlson

GÖTEBORG 1969
ELANDERS BOKTRYCKERI AKTIEBOLAG

CONTENTS

The present work is in some parts based on the following publications

I Power Spectra of Myoelectric Signals in Muscles of Arm Amputees and Healthy Normal Controls
Herberts P Kaiser E Magnusson R & Petersen I Acta orthop scand In press

II Electrodes for Myoelectric Control of Prostheses
Kadefors P Herberts I Hirsch C Kaiser E & Petersen I Medicinsk teknik—Medicoteknik 1 43 1968

III Implantation of Microcircuits for Myoelectric Control of Prostheses
Herberts I Kadefors R Kaiser E & Petersen I J Bone Jt Surg 0 B No 4 780 1968

IV Measurement and Evaluation of Myoelectric Control in a Man Machine System
Herberts I Kaiser E & Petersen I Medicinsk teknik—Medicoteknik 1 9 1968

The papers are referred to in the text by their Roman numerals

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INTRODUCTION

As a result of the great number of traumatic injuries to the extremities during World War II there was a renewed interest in various types of prostheses. During latter decades great importance has been attributed to the rehabilitation of patients with impaired motor function by means of orthoses. Prostheses and also orthoses were previously designed so that the force required by the device had to be mobilized by the patient. The standard method of controlling the conventional prostheses and orthoses in the upper extremities is a mechanical control by gross body movements of the trunk and the extremities transmitted by means of cables attached to the harness. This type of mechanical control is disadvantageous mainly because the force of the movements in the prosthesis will be limited, the range of motion will be small and at the same time the necessary movements will cause the patient discomfort and fatigue. Furthermore the functions of the prosthesis are limited as several movements cannot be performed simultaneously without important parts of the body being bound to the control function in a very disturbing way.

Advanced technical research has permitted the design of new types of prostheses and orthoses which are supplied with an external source of power. Already in 1919 a method of converting electric power into mechanical movements in prostheses was published (*Borchardt & Schlesinger* 1919). During the interwar period this type of prosthesis and similar designs were unpractical because of their weight and the difficulties for the patients to control them adequately. Two different sources were later utilized to deliver power to the prostheses and the orthoses, i.e. pneumatic and electric power. For pneumatic power liquid carbon dioxide was used, for instance, in "The Heidelberg pneumatic arm prosthesis" (*Weil* 1959) and "The Hendon pneumatic prosthesis motor" (*Kinnier Wilson* 1960). The great advantages of pneumatic prostheses as compared to electric were their smooth, comparatively noiseless running and their light weight.

During World War II and the following wars there was a renewed interest in prostheses equipped with external power. Towards the end of World War II *Wilms* in Berlin began designing an electric hand prosthesis which later has developed into the so-called French electric hand (*Lucaccini, Kaiser &*

Lyman 1966) Research of many years duration began in the USA in 1946 to design an electric arm prosthesis which finally resulted in five different types (*Alderson* 1954) A common phenomenon in these American models was that only a few control movements were required of the amputee to release multiple sequentially coded movements in the prosthesis This proved to be unnatural for the patient and a considerable amount of practice was required before the amputees could use these prostheses Thus they were not generally accepted The great problem has been to enable the patients to control prostheses and orthoses which are operated by external power The difficulties become even greater with complicated devices having more degrees of freedom For each direction of motion the action as a rule demands one control site *i e* a part of the body from which control impulses can be picked up

The control of the first electric prostheses introduced after World War II was carried out mechanically by wires or by utilizing the change in volume to which a muscle is subjected when contracted Mechanical transducers were fitted in the socket of the prosthesis causing an impulse when the amputee contracted his stump muscles *Berger* & *Huppert* (1952) first suggested that in order to obtain a better control of the externally powered prostheses the electric signals generated in connection with muscular contraction should be used as a control signal Originally this possibility was mentioned by *Wiener* (1947) who pointed out that myoelectric signals could be detected in the stump muscles of arm amputees and that these signals would probably allow control of a prosthesis (*Bottomley* 1965) The release of myoelectric signals—in voluntary contraction—is via central and peripheral neurons controlled by the brain Advantage is taken of this fact when utilizing myoelectric signals for prosthesis control This type of control will thus be experienced by the amputee as more natural than the conventional mechanical control (*McLaurin* 1965) Furthermore no extensive and disturbing movements of the body are demanded less muscular force is required and the risk of the patient becoming fatigued is reduced A further important fact is that the patient will receive proprioceptive impulses from the muscles involved giving a sensation of communication with the prosthesis (*Popov* 1965 *Scott* 1966)

In arm amputees and patients with impaired motion due to pareses of different origin the myoelectric signals often differ in appearance The frequency and degree of these changes in various muscles of arm amputees are discussed in this paper Furthermore the ability of arm amputees and normals to utilize their myoelectric signals as control impulses and the electrode problems involved in picking up these signals have been studied

HISTORICAL REVIEW

Arm Amputees

Although the history of prostheses is closely connected with the years following the two great World Wars the number of amputations in civilians considerably exceed that in disabled soldiers As a result of the War 1941–194[illegible] the number of arm and leg amputations in the USA was estimated to be 40 000 while for civilians the corresponding number a few years ago was 500 000 (*Aller* 1966) In the same country the total number of recent amputations was approximately 3[illegible] 000 per annum (*[illegible]ussel* 1961) The British Ministry of Health compiles all annual amputations also including frequency age sex and etiology These reports are forwarded by the prostheses workshops During a number of years this has enabled the relation between arm and leg amputees to be determined the ratio being one to ten At the same time an annually increased frequency of new amputations could be observed in Great Britain in agreement with a series of leg amputations in Sweden examined by *Hansson* (1964)

In 1962 Great Britain thus registered approximately 300 fresh arm amputations Based on the frequency of fitted prostheses the rate of annual leg amputations in Sweden was recently estimated at 1000 cases (*Herberts* 1968) The number of new arm amputations in that type of study is more difficult to determine but the frequency of cases was assessed at 100 per annum which also resulted in a relation of one to ten between arm and leg amputees The total number of arm amputees in Sweden was estimated at 900 patients by the Swedish Committee for Disabled in 19[illegible] while the frequency at present could be estimated at 1500

The difference in sex is obvious among arm amputees inasmuch as the males are in the majority Thus *Watkins & Ford* (1962) in a follow up of 1[illegible]0 arm amputees found five times more males than females The male predominance among arm amputees was also noted by *Hansson* (1966) who in a study on 243 arm prosthesis applications found nine males to one female

Contrary to leg amputation the loss of an arm generally strikes young people Several series reveal that most of the patients are younger than 50 years of age at the time of accident the mean age ranging from 20 to 30 years (*Watkins & Ford* 1962 *Hansson* 1966)

Lyman 1966) Research of many years duration began in the USA in 1946 to design an electric arm prosthesis which finally resulted in five different types (*Alderson*, 1954) A common phenomenon in these American models was that only a few control movements were required of the amputee to release multiple sequentially coded movements in the prosthesis This proved to be unnatural for the patient and a considerable amount of practice was required before the amputees could use these prostheses Thus they were not generally accepted The great problem has been to enable the patients to control prostheses and orthoses which are operated by external power The difficulties become even greater with complicated devices having more degrees of freedom For each direction of motion the action as a rule demands one control site i e a part of the body from which control impulses can be picked up

The control of the first electric prostheses introduced after World War II was carried out mechanically by wires or by utilizing the change in volume to which a muscle is subjected when contracted Mechanical transducers were fitted in the socket of the prosthesis causing an impulse when the amputee contracted his stump muscles *Berger* & *Huppert* (1952) first suggested that in order to obtain a better control of the externally powered prostheses the electric signals generated in connection with muscular contraction should be used as a control signal Originally this possibility was mentioned by *Wiener* (1947) who pointed out that myoelectric signals could be detected in the stump muscles of arm amputees and that these signals would probably allow control of a prosthesis (*Bottomley* 1965) The release of myoelectric signals—in voluntary contraction—is via central and peripheral neurons controlled by the brain Advantage is taken of this fact when utilizing myoelectric signals for prosthesis control This type of control will thus be experienced by the amputee as more natural than the conventional mechanical control (*McLaurin* 1965) Furthermore no extensive and disturbing movements of the body are demanded less muscular force is required and the risk of the patient becoming fatigued is reduced A further important fact is that the patient will receive proprioceptive impulses from the muscles involved giving a sensation of communication with the prosthesis (*Popov* 1965 *Scott* 1966)

In arm amputees and patients with impaired motion due to pareses of different origin the myoelectric signals often differ in appearance The frequency and degree of these changes in various muscles of arm amputees are discussed in this paper Furthermore the ability of arm amputees and normals to utilize their myoelectric signals as control impulses and the electrode problems involved in picking up these signals have been studied

performed on the indication of a tumour. As most of the arm amputations are the result of a trauma, it is comprehensible that the remaining muscles, nerves and other tissues may reveal changes in an amputated extremity. These changes are not merely localized to the stump area; there may also be severe pathological changes proximally in the injured extremity due to traction of the nerves and vessels at the time of the accident.

Myoelectric Control Systems

It was three British scientists, *Battye, Nightingale & Whillis* (1955), who again suggested that myoelectric signals should be possible to utilize for control of prostheses and who introduced a by now classic description of a myoelectric control system. They proved that below elbow amputees could actively control prehension in a simple prosthesis by myoelectric signals produced in the stump muscles. Patients recently operated upon were considered to control the prosthesis with less difficulty than those earlier amputated. The new technique of the transistor made the work with electronic control systems more attractive than before. Disturbances in the myoelectric signals from the external surroundings, from the skin electrodes and from the amplifiers were pointed out. A few years later a myoelectrically controlled hand prosthesis was developed in the Soviet Union (*Kobrinski et al.* 1960). In both these prosthesis systems skin electrodes were utilized to pick up the myoelectric signals. The Russians have applied their hand prosthesis in at least 1000 patients (*Lymark* 1968) and it has also been sold on a licence for clinical application to Great Britain (*McKenzie* 1965) and Canada (*Sherman* 1964, *Gingras et al.* 1966). This prosthesis lacks active pronation and supination and does not offer any proportional grip. It is easy to subscribe to the favourable points raised by *Scott* (1966) about the Russian electric hand having been released for clinical use and criticism which allowed valuable practical experience to be gained. *Gingras et al.* (1966) found the technical design incomplete and modified several components on the basis of their experience.

In the beginning of the 1960's a number of myoelectrically controlled hand prostheses were introduced (*Horn* 1963, *Bottomley & Cowell* 1964, *Hirsch, Kaiser & Petersen* 1964, *Schmidt* 1965, *Knowles, Stevens & Howe* 1965). All these systems merely offered one function, prehension. Skin electrodes were used to pick up the myoelectric signals, and the remaining extensor and flexor muscles of the forearm stump were utilized as control sites. The brachial biceps and triceps muscles and other groups of muscles have also been suggested. No proportional control of the grip could be offered with these prosthetic systems. A few attempts have been made to obtain control of more functions than pre

Etiological studies of arm amputations show that most cases were caused by trauma. Thus in 60–84 per cent of the cases trauma was the cause of the patient's handicap. Following trauma, congenital aplasia commonly resulted in amputation, whereas malignant tumours amounted to less than 10 per cent, as is shown in Table 1. The traumatic lesions were mostly due to industrial accidents. During 1962 in Great Britain traumatic arm amputations were reported to be caused by industrial accidents in 60 per cent, whereas approximately 20 per cent were due to traffic accidents.

Table 1. Causes of amputation in two series

	No. of cases	Trauma	Congenital defect	Tumour
Great Britain acc. to Brit. Ministr. of Health 1962	296	60%	27%	6%
Gothenburg, Sweden, acc. to Hansson 1966	74	72%	16%	8%

In principle, arms can be amputated at six functionally different levels. The level of amputation is decisive for the degree of loss of function and the resulting handicap. In exarticulation of the wrist there generally remains a satisfactory pronation and supination ability, but there is lack of prehension. In exarticulation of the shoulder, of course, no function whatever remains. The amputation levels found in patients on five different investigations are indicated in Table 2. It should be noted that *Muller* (1962) and *Nathan* &

Table 2. Levels of amputation in different investigations

	Forequarter	Above elbow	Below elbow
Muller 1962	5	31	26
Watkins, Ford 1962	[illegible]	46	81
Nathan, Davidoff 1965	—	19	17
Solonen *et al.* 1965	—	24	48
Hansson 1967	—	16	52

Davidoff (1965) and *Solonen* (1965) performed their investigations on disabled soldiers. In the two remaining series—representative of a country in peace—there was a significant predominance of below elbow amputees. Extensive exarticulations of the shoulder joint are rare as these operations are mainly

vance in prosthetic research was made when a prosthesis model was introduced which could utilize the myoelectric signals for proportional control of pneumatic as well as electric power supplies (*Bottomley* 1962 *Bottomley Kinnier Wilson & Nightingale* 1963) *Bottomley & Cowell* (1964) reported a method to obtain proportional control of a myoelectrically controlled split hook Skin electrodes were used to receive myoelectric signals from the forearm extensors and flexors and the difference signal (*Bottomley et al* 1963) between the electrodes was utilized to control both the speed of movement and the force of grip when the hook opened and closed This was achieved by two feed back signals one of which depended on the speed and the other on the force of grip The clinical observation on which this solution was based is that a hand at work either opens or closes without using any force or grips with force without moving The effect of the random variations on the myoelectric signals can be considerably reduced by applying a so called back lash generator (*Bottomley et al* 1963) This method permits a great variation in the myoelectric signals without reducing the ability to control the hand when loaded lightly In Great Britain the technical development of this hand has been transferred to the Atomic Weapons Research Establishment but no clinical results of prosthetic applications on amputees have as yet been published

In recent years it has been stated that an improved hand function can be obtained by certain elements of the electric hand prostheses performing automatically An adaptive grip is offered (*Tomovic* 1961 1962 *Palic* 1964 1968) by placing several pressure sensitive transducers on the finger tips and palms of the hand which when activated transmit a feed back signal to the prosthesis The hand will then automatically perform a number of standard movements depending on the transducers involved This hand according to the latest modification can instead of the conventional stiff three finger grip perform a forceful grip towards the palm of the hand hook grip and clenching of the hand (*Lymark* 1968) Another type of feed back from the prosthesis to the carrier has been described where a pressure sensitive crystal situated on the prosthesis thumb gives an electric signal when deformed (*Beeker During Vden Hertog* 1967) The purpose of this signal was to achieve cutaneous stimulation in one part of the body via surface electrodes At present the advantage of the transmitted sensibility is being tested on a number of amputees An extensive investigation of different methods to offer the amputee communication with the prosthesis via the tactile senses was recently published (*Illes* 1968)

One of the primary problems arising in the development of myoelectric control systems is no doubt the lack of muscle control sites which has also been emphasized by *Croth Weltman & Lyman* (1962) The lack of sites i e the fact that there are few places in the body where a control signal is available

hension (*Lyman Groth & Weltman* 1964) So far nobody has managed to control three degrees of freedom (*Godden* 1968 among others) despite many years research activities still going on in several laboratories

Geddes Moore Spencer & Hoff (1959) introduced the use of myoelectrically controlled orthoses Via myoelectric signals from a forearm muscle a pneu matic orthosis applied to a paralytic hand could be controlled Myoelectric control of electric orthoses has later been developed utilizing signals from a paretic muscle (*Waring & Nickel* 1965 *Antonelli & Waring* 1967 *Waring & Antonelli* 1967) The low level of myoelectric signals which can be picked up in severe paresis demands a high sensitivity of the amplifier in order to obtain a sufficient signal to noise ratio In connection with orthoses paretic muscles were electrically stimulated This method was initially utilized by stimulation of the peroneal nerve in hemiplegics with a drop foot (*Liberson et al* 1961) Electric stimulation of paretic muscles in the upper extremities was later described which enabled a paretic hand to perform an active movement (*Long & Masciarelli* 1963) In this case the paretic forearm extensors were electrically stimulated via skin electrodes and the hand splint fitted to the patient was closed by means of a spring The patient s active control over the so called electrophysiological hand splint was mechanical via remaining non paretic muscles of the shoulder Myoelectric control was later developed where instead of mechanical control the signals from intact shoulder muscles were utilized to control the hand splint (*Resuick & Vodoinik et al* 1964 *Vodoinik et al* 1965) The system was designed so that the amplitude of the myoelectric signals which were utilized as control signals were proportional to the ampli tude of the stimulating impulse which affected the paretic muscle *Crochetiere Vodoinik & Resuick* (1967) have shown that a rectified rectangular stimulating impulse is the most favourable and that the stimulating electrode should be large because of the muscular response to the stimulation *Vodoinik Croche tiere & Resuick* (1967) also reported that the position of an extremity could be determined as a function of the amplitudes of the stimulating impulses

There are in principle two different methods of myoelectric control of prostheses *on off or threshold control* and *proportional control* In the first case there will be an indication if the signal amplitude exceeds a certain threshold level which is sufficiently high to prevent effectively disturbances caused by noise induction or resting potentials Proportional control implies that the signal is satisfactorily reproducible and that it will not be affected to a great extent by fatigue hysteresis or artefacts *It has been pointed out* that the intensity of the myoelectric signal on the whole varies continuously *with the muscular tension* (*Lippold* 1952 *Bigland et Lippold* 1954) There fore if the myoelectric signal is only utilized for on off control of the prosthesis a great deal of signal information will never be extracted An important ad

offer a solution to the control problem (*Bottomley* 1965 *Scott* 1966) Audial and visual feed back after training permits normal subjects to control up to three motor units in one muscle in a few cases even more (*Basmajian Baeza & Fabrigar* 1965) Certain subjects can maintain the control over single motor units even without artificial feed back The total number of units which can be activated irrespective of each other has not yet been determined Using this method it is possible that several control sites can be obtained from a single muscle to control the prosthesis *Harrison & Mortensen* (1962) believe that the frequency of the single motor unit activity also can be controlled voluntarily *Wagman & Pierce* (1966) pointed out that with the technique described the remaining muscle is relaxed when the single motor unit is activated No attention has been paid to the extent of which the single motor unit has participated in the total muscle contraction Recently it has been pointed out however that subjects can be trained to maintain control over and alter the frequency of single motor units in a muscle even when certain disturbing movements occur in the extremity which is actuated by the muscle involved (*Basmajian & Simard* 1967)

Electromyography

During the middle of the 18th century the first reports were given of muscle contractions evoked by static electricity stimulation (*Kratzenstein* 1746) The most renowned investigation showing the connection between electricity and muscle contractions was a series of studies on frog muscle (*Galvani* 1791) The animal electricity was not believed by *Galvani* to originate from muscles but from nervous tissue particularly the brain It was not until 1838 that it was shown that electric current really was developed in muscles (*Matteucci* 1844) The first to pick up electric current in active muscle contraction in man the first human electromyogram was *DuBois Peymond* in 1851 (*Licht* 1961) In the beginning of the 20th century improved methods were introduced inter alia by means of a string galvanometer (*Einthoven* 1901) which permitted rapid and sure recording of the weak electric activity accompanying muscle contraction

Electromyography (EMG) the recording of an electric phenomenon in striated muscles was then employed mainly by physiologists The first to apply this technique on pathological cases was *Proebster* who in 1928 studied a number of peripheral neuron lesions At about the same time *Adrian & Bronk* (1929) introduced a concentric needle electrode to be inserted into the muscle During the following years clinical electromyography was developed as a diagnostic aid in the studies of pareses and atrophy both of muscular (*Lindsley* 1935 *Kugelberg* 1947 1949) and neurogenic origin (*Denny Brown & Pennybacker*

reduces the possibility for the patient to communicate with the orthosis or prosthesis. It has been mentioned (*Bottomley* 1965, *Scott* 1966, 1967) that to those who are severely handicapped, unilateral or bilateral amputees, myo-electric control will be of the greatest advantage. The paradoxical situation then arises that the patients who are in the greatest need of a prosthesis with several degrees of freedom have a less number of well conducted muscle control sites available. It is obvious that the advantage of the normal hand as a gripping tool depends on its ability to perform in an adequate position (*Capener* 1960). A prosthesis with several degrees of freedom would therefore be desirable. The myoelectrically controlled hand prostheses available so far offer one function only—prehension—and no proportional control. By picking up three amplitude levels in the contraction of one separate muscle, two control sites will be available in one muscle (*Dorcas & Scott* 1966) and the demand of multiple control sites will be reduced. Only a little practice allows separate control of both functions, opening and closing of the hand. *Scott* (1966) mentioned that sufficient signals to control this three state unit can be picked up from partially denervated and atrophic muscles in amputees. Due to the lack of a description on the pathologically disturbed myoelectric signals, the magnitude of these changes cannot be assessed.

Programme coding of prosthetic function is another form of reducing the number of control sites for the control of complicated prostheses and orthoses. The prosthesis will then have certain automatic movements. A sequential coding equals a series of movements released by one single control site, which technically can act very naturally (*Waling & Clarkson* 1963). This system, however, is slow and requires continual attention and cannot be unconsciously controlled by the patient. A better system is parallel coding where a number of control sites are activated in various pattern combinations synchronously. By comparing control signals, various codes in a pattern detector can be combined and the prosthesis can operate in several degrees of freedom simultaneously (*Michael & Crawford* 1963, *Harrison* 1964). This parallel coding will increase the number of functions available from a given number of muscles. Signals from strain gauges are sometimes used to indicate a muscle contraction instead of myoelectric signals (*Lyman, Groth & Weltman* 1964). Attempts were made to obtain control of an arm simulator with three degrees of freedom (*Lucaccini, Freedy, Rey & Lyman* 1967).

Muscles which normally do not have any specific function, for instance the auricular muscles, can be trained to give voluntary contractions (*Bontrager* 1965). It is doubtful whether this type of myoelectric control will turn out to be of any practical value, since too much effort is demanded of the patient.

The fact that the human being can control single motor units voluntarily in a muscle (*Harrison & Mortensen* 1962, *Basmajian* 1963) was believed to

an individual motor unit are dispersed within an area constituting 17 per cent of the sectional area of the rat muscle with a considerable overlapping between different units. When a nerve impulse reaches the motor endplate where the terminal axon fibres are close to the separate muscle fibres the cell membrane of the muscle fibre will be gradually depolarized. At a certain level the action potential becomes released as a result of the instantaneous change of the membrane potential. This depolarization continues along the muscle fibre at a rate of 4–5.5 m/s in the human brachial biceps muscle according to *Buchthal, Guld & Rosenfalck* (1955), 3–4 m/s according to *Stålberg* (1966). The speed of dispersion along the muscle fibre becomes reduced in ischaemia and at a low intramuscular temperature (*Stålberg* 1966). Following the depolarization of the muscle fibre membrane the muscle fibre contracts. The problem of the relation between excitation and contraction, however, is still not solved. The brief contraction of the individual muscle fibre lasts from 1 to 2 msec and during the same time an electric potential is spread in the surrounding tissues as a result of the depolarization. The existence of different motoneurons with different functions, so called phasic and tonic motoneurons, was demonstrated on cat (*Cranit, Henatsch & Steg* 1956, *Eccles, Eccles & Lundberg* 1958). By means of histochemical methods it has recently been proved on rat that with respect to function there are different muscle fibres and motor units (*Kugelberg & Edström* 1968, *Edström & Kugelberg* 1968).

Motor Unit Action Potential Parameters

The purpose of diagnostic electromyography is to determine exact, quantifiable and reproducible criteria of the myoelectric activity of the muscles in various known metabolic disturbances and diseases. For this quantitative measurements of various parameters of the individual motor unit potential have mainly been used, such as duration, shape and amplitude. The parameter which is considered as the most favourable and also offers the best information in pathological conditions of the muscle is the duration of the motor unit potential. The duration of the motor unit potential is longer than that of the individual muscle fibre (*Buchthal, Guld & Rosenfalck* 1954). This depends on the muscle fibres of the same motor unit having a certain territorial dispersion and an almost simultaneous activation, which results in a temporary dispersion. The electric potential which can be picked up from the motor unit has a duration of 7–8 msec in the human extremity muscles (*Buchthal & Clemmesen* 1941, *Petersén & Kugelberg* 1949) and an amplitude between 0.1–0.5 mV. During latter years duration measurements according to stipulated criteria (*Buchthal & Rosenfalck* 1955) resulted in higher values, thus in the human brachial biceps a duration of 9–10 msec was reported (*Kaiser &

backer, 1938 *Buchthal & Clemmesen* 1941) Several compilations of the EMG changes, found by employing electromyography in different pathological conditions have been made (*Wedell Feinstein & Pattle* 1944 *Buchthal & Pinelli* 1952) With the increased information gained by electromyography this method has now become a clinical routine Furthermore during recent decades electromyography has come into use for anatomical and kinesiological studies of the muscular function (*Basmajian* 1967) Several surveys have been published (*Kugelberg* 1953 1959 *Isch* 1963 *Buchthal* 1957 1960 1961 *Licht* 1961 *Basmajian* 1967)

The Motor Unit

In the muscle the structural unit is constituted by the muscle cell or the muscle fibre The human muscle fibre varies considerably in length in different muscles the mean value being about 50 mm (*Lindhard* 1931) There is also a difference in diameter of the muscle fibres ranging from 0 03–0 1 mm with a smaller diameter in small muscles such as the external ocular muscles A number of muscle fibres are innervated by the same motor nerve fibre or axon originating from one anterior horn cell of the spinal cord This nerve cell with its axon and terminal branches as well as the innervated muscle fibres form an anatomical and functional unit the motor unit (*Sherrington* 1925) The nerve fibres divide close to the muscle fibres and do not spread over the entire muscle but the contact between the nerve fibre and the single muscle fibre occurs within the so called endplate zone in the middle area of the muscle fibre (*Coers* 1953 *Coers & Woolf* 1959) This endplate zone is well demarcated and constitutes less than 10 per cent of the total length of the muscle (*Buchthal Guld & Rosenfalck* 1955) The number of muscle fibres per motor unit differs considerably in each muscle Muscles controlling precise and rapid movements generally have the smallest number of muscle fibres per motor unit Thus in man there are ten fibres per unit in the tensor tympani muscle (*Wersall* 1958) as opposed to 1600 in the medial head of the gastrocnemius muscle (*Feinstein Lindegard Nyman & Wohlfart* 1955) The remaining muscles range between these extreme values

The muscle fibres belonging to one motor unit are dispersed over a certain area and mingled with fibres connected with other motor units demonstrated by means of a multi electrode technique elaborated by *Buchthal Guld & Rosenfalck* (1957) Fibres relating to the same motor unit have been demonstrated in circular areas with a diameter of 5–7 mm in the upper extremities and 7–10 mm in the lower extremities These areas allow space for muscle fibres from 15–30 different motor units (*Buchthal Erminio & Rosenfalck* 1959) *Edstrom & Kugelberg* (1968) recently reported that the fibres of

tion is obtained This activity probably caused by mechanical irritation generally appears in showers (*Buchthal & Clemmesen* 1941) and sometime can be observed during several minutes (*Petersen & Kugelberg* 1949) When the muscle contraction is weak individual motor units are activated at the lowest possible frequency of 5–10 per sec In higher muscle contraction more and more units are gradually activated and the discharge frequency of the individual unit increases in man up to approximately 50 per sec (*Adrian & Bronk* 1929) An average maximum frequency has later been indicated at 20 per sec (*Wedell Feinstein & Pattle* 1944) and 25 per sec (*Basmajian et al* 1965) As gradually more and more units are added a complex pattern is obtained and the individual motor unit potentials can no longer be identified

Pathological Changes in EMG

Atrophy of the muscles and pareses of varying degrees may be caused by disease and damage affecting the lower motoneuron or the muscle Both in neurogenic and myogenic pareses there are characteristic changes in the electromyogram with respect to the individual motor unit potential and the signal pattern on higher levels of contraction This also applies to the appearance of spontaneous electric activity of the muscle In peripheral motoneuron lesions with muscle denervation spontaneous fibrillar action potentials can be recorded from the relaxed muscle about 2–3 weeks following the lesion (*Denny Brown & Pennybacker* 1938) These potentials have a short duration of 1–2 msec and are considered to reflect the activity of individual muscle fibres They appear at a low frequency The fibrillation potentials however occasionally can be observed in non denervated muscles Consequently the finding of fibrillar action potentials must be carefully assessed in connection with the diagnosis Another type of potential appearing in relaxed denervated muscles is repetitive with an introductory so called positive phase and a duration of 4–8 msec (*Kugelberg & Petersen* 1949 *Jasper & Ballem* 1949) In affection of the anterior horn cells of the spinal cord large polyphasic potential appear corresponding to the fasciculation which can be seen with the naked eye (*Pinelli & Buchthal* 1953) In peripheral neuron lesion the number of activated motor units can be reduced at a maximum muscle contraction (*Buchthal* 1957) Often the activity does not fill the base line and sometimes only single units are recorded Furthermore in about 50 per cent of the cases the duration becomes prolonged (*Buchthal & Clemmesen* 1941) and usually there is an increase in the amplitude of the motor unit potential (*Denny Brown & Pennybacker* 1938) This can partly be explained by the regenerating nerve fibres not only contacting muscle fibres within their own motor unit but also others (*van Harreveld* 1945) and by an in

Petersen 1965) The duration of the motor unit potential varies considerably within different muscles Muscles with fewer fibres per motor unit for instance the facial muscle have a decidedly shorter duration than muscles with more fibres per motor unit (*Petersen & Kugelberg* 1949) This can partly be explained by the reduced temporal dispersion which is found with a less number of fibres per unit (*Buchthal & Rosenfalck* 1955) The density of the fibres is of importance for the duration of the motor unit potential The duration of the motor unit potential depends on the type of electrodes used which must be indicated and standardized (*Petersen & Kugelberg* 1949) With increasing age the mean duration of the potential will become prolonged (*Petersen & Kugelberg* 1949 *Buchthal & Pinelli* 1952) There will also be a prolongation of the mean potential duration when the intramuscular temperature drops (*Bentsen* 1945 *Buchthal & Pinelli* 1952) The same muscle reveals a deviating duration of various motor unit potentials as a result of different distances between the electrode and the endplate zone (*Buchthal Guld & Rosenfalck* 1954 *Kaiser & Petersen* 1965) A shorter duration has been indicated for the long head of the biceps muscle as compared to its short head (*Kaiser & Petersen*, 1963 1965) These authors stated that the mean duration is slightly longer for males than females

The individual motor unit potential may appear in a mono bi or tri phasic form, depending on the type of electrode Due to the scattering of individual fibres in the motor unit poly phasic potentials also appear and an increased spatial and temporal dispersion causes an increase in the number of poly phasic potentials (*Buchthal* 1960) In muscles where the motor unit potential has a long duration, there are thus more poly phasic potentials than in muscles with a short motor unit potential (*Buchthal Guld & Rosenfalck* 1954) The number of poly phasic potentials also increases pronouncedly at a low intramuscular temperature and also in connection with fatigue (*Buchthal Pinelli & Rosenfalck* 1954)

The third parameter studied in the motor unit potential is the amplitude The amplitude is dependent on the fibre density and the number of muscle fibres of each motor unit and will increase linearly with the territorial magnitude of the motor unit (*Buchthal Erminio & Rosenfalck* 1959) The amplitude varies noticeably with the types of electrodes and the depths of insertion into the muscles i e the distance to the active muscle fibres On the other hand it has been stated that the muscle temperature only has an insignificant effect and that fatigue does not at all affect the potential amplitude (*Buchthal Pinelli & Rosenfalck* 1954)

In a relaxed normal muscle no electric activity can be demonstrated (*Adrian & Bronk* 1929 *Lindsley* 1935) When a needle electrode is inserted into a normal relaxed muscle a repetitive insertion activity of a short dura

tion is obtained. This activity probably caused by mechanical irritation generally appears in showers (*Buchthal & Clemmesen* 1941) and sometimes can be observed during several minutes (*Petersen & Kugelberg* 1949). When the muscle contraction is weak individual motor units are activated at the lowest possible frequency of 5–10 per sec. In higher muscle contraction more and more units are gradually activated and the discharge frequency of the individual unit increases in man up to approximately 50 per sec (*Adrian & Bronk* 1929). An average maximum frequency has later been indicated at 20 per sec (*Wedell, Feinstein & Pattle* 1944) and 25 per sec (*Basmajian et al.* 1965). As gradually more and more units are added a complex pattern is obtained and the individual motor unit potentials can no longer be identified.

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creased synchronization (*Buchthal & Honcke* 1944) An early sign of re inner vation may be the cessation of the fibrillation potentials or the appearance of poly phasic potentials (*Wedell Feinstein & Pattle* 1944 *Jasper* 1946)

In diseases of a muscle myogenic atrophy or pareses myosites or meta bolic toxic and degenerative lesions of the muscles the motor unit becomes changed by a gradual destruction of individual muscle fibres while the number of motor units remains intact (*Kugelberg* 1947 1949) When the level of muscle contraction is high the number of motor unit potentials picked up is large in proportion to the pareses and fills the base line This is characteristic of advanced muscle dystrophy and is different from neurogenic pareses since in paresis of a corresponding degree a reduced number of motor units will be activated at maximum contraction The duration of the individual motor unit potential is often greatly reduced in myogenic pareses and moreover there is an increased number of poly phasic potentials (*Kugelberg* 1947 1949 *Buchthal & Pinelli* 1952 *Pinelli & Buchthal* 1953 *a*)

Frequency Analysis

Detailed investigations of the individual motor unit potential including duration measurements require that the level of contraction in the muscle be low In this case a few well isolated potentials can be picked up As the level of contraction rises an increasingly complex signal is recorded which unables further study of individual potentials The question then arises whether measurements of isolated potentials in connection with weak con tractions will offer values representative of all motor units It is thus desirable to analyse the myoelectric signal for high levels of contraction also

Piper (1907) was the first to apply frequency analysis to the study of myo electric signals in voluntary contraction He found that the signal amplitude varies regularly at a frequency of 47 to 50 Hz the so called Piper rhythm It was not until 1951 that the relation of various components in the power spectrum of the myoelectric signal was studied by a simple method (*Richard son* 1951) *Richardson* determined the relation between power spectrum com ponents above and below 400 Hz Increased signal activity at high frequencies was believed to indicate myopathy A frequency analyzer was first used to describe the power spectrum in detail both in normal and pathological cases by *Walton* (1952) The analysis of normals revealed a predominating activity between 100 and 250 Hz which gradually declined with increasing frequency and essentially vanished at 800 Hz It was only in the facial muscle and the small hand muscles that frequencies up to 1250 Hz could be observed In myopathy the predominating activity of the myoelectric signal was displaced towards higher frequencies Peripheral neuron lesions on the other hand

caused no changes in the power spectrum. These results have later been confirmed (*Fex & Krakau* 1957).

Neurogenic and myogenic atrophy were believed by these authors to change the shape of the power spectrum, particularly involving frequency displacements of the spectrum peak. A certain displacement toward higher frequencies could be observed in inactivation atrophy. This is in accordance with the fact that the duration of the individual motor unit potential is shorter in these cases (*Buchthal & Pinelli* 1952). Contrary to earlier investigations it has later been proved (*Kopec & Hausmanowa-Petrusewicz* 1966) that in peripheral neuron lesions also the power spectrum of the myoelectric signals alters. Thus the spectrum will be more compressed and will decline rapidly both at low and—even more pronouncedly—at high frequencies.

The power spectrum of the myoelectric signal depends on the choice of electrode. The activity picked up with needle electrodes contains components of higher frequencies than that obtained with skin electrodes. This is partly due to the change imposed on the motor unit potential as it is transmitted through the tissues and picked up by a large electrode (*Fex & Krakau* 1958). The power spectrum is also dependent on the positioning of the skin electrodes, the distance between the electrodes and the angle between the direction of the electrode and the muscle fibres (*Sato* 1964). As the electric fields in the various motor units differ in amplitude, phase, repetitive frequency and polarity, the individual motor unit potentials will add randomly at the electrode (*Haye* 1960). At higher levels of contraction the myoelectric signal therefore assumes the essential characters of noise. When the levels of contraction rise the motor unit potentials become synchronized, which results in increased potential duration and amplitude (*Krakau* 1958). The low frequency components of the power spectrum are thus augmented. This synchronization which has been described earlier (*Buchthal & Clemmesen* 1941) probably is the origin of the Piper rhythm. It has been stated that the predominating frequency of the power spectrum is different for different muscles (*Sato & Tsurumi* 1967). These authors found the predominating frequency range of the human brachial biceps muscle to be 50 to 60 Hz, as opposed to that of the gastrocnemius muscle which was stated to be 100 to 200 Hz. Other authors have found the power spectra of the myoelectric signals in various muscles to be rather similar (*Fex & Krakau* 1958). In Paper I (*Herberts, Kaiser, Magnusson & Petersén* 1969) however a great number of statistically significant intermuscular differences have been demonstrated. Changes in shape of the low frequency portion of the power spectrum due to changes in contraction level have also been observed (*Kaiser & Petersén* 1963). *Kaiser & Petersén* (1963) were the first to find that the signal activity at frequencies exceeding 1000 Hz declined during a constant maximum contraction. They also intro

duced a method of describing the profile of the spectrum with points in a frequency coordinate system i e loci Six filters suffice to give an accurate description of the frequency profile

Several investigations have been made dealing with the influence of fatigue on the appearance of the normal myoelectric signal It has been pointed out that the signal pattern in isometric contraction probably deviates from that in ergometric work (*Scherrer & Bourguignon* 1959) In forceful isometric muscle contraction the myoelectric signal alters as a function of time during a prolonged contraction The fact that prolonged muscle contraction reduces the amplitude of the motor unit potentials was mentioned as early as 30 years ago (*Seyffarth* 1940) Since then skin electrodes have been used to demonstrate that a fatiguing muscle contraction is accompanied by an increase in the myoelectric amplitude due to synchronization of the potentials Consequently there will be a displacement of the power spectrum towards low frequencies (*Sherrer & Bourguignon* 1959) Frequency analysis also revealed that the amplitude increase in connection with muscle fatigue was concentrated to the low frequency part of the spectrum (*Kogi & Hakamada* 1962) These changes picked up by skin electrodes were considered to be caused by the synchronization of motor units The existence of synchronization has been proved by means of cross correlation analysis (*Person & Kudina* 1968) An extensive investigation of dynamic changes in the power spectrum of the myoelectric signal during fatiguing muscle contractions was recently published by *Kadefors Kaiser & Petersen (1968) During* an *isometric isotonic* fatiguing contraction of the brachial biceps muscle there is a significant increase of the total myoelectric signal activity The spectral changes are increased activity within the low frequency band and reduced activity within the high frequency band These effects do not occur simultaneously and are probably of different origin Synchronization and activation of further motor units may explain the total increase in the signal activity and a drop out of particular motor units may explain the reduced activity within the high frequency range Analyses of high speed registrations of the myoelectric signal *support this theory* These findings are of particular interest in conjunction with the previously mentioned possibilities of separating functionally different kinds of motor units

Electrodes

Bioelectrical electrodes of various types are used for the following three main purposes impedance measurement bioelectric signal pick up and stimulation In picking up myoelectric signals there are three methods of placing the electrodes on the skin percutaneously and subcutaneously The electrodes

employed are correspondingly called skin electrodes percutaneous and implantable electrodes In all myoelectric control systems so far introduced for clinical use skin electrodes are employed and have been believed to be the only practical solution (*Alter* 1966)

There are two classes of skin electrodes wet and dry electrodes The dry ones consist of a metal plate fitted to the skin whereas the wet ones are supplied with an electrolytic layer between the skin and the metal plate This classification is not quite adequate since the dry electrodes also become covered with a thin electrolytic layer when they are applied to the skin One disadvantage which is more pronounced in dry than wet skin electrodes is the high level of impedance about 100 kohm Thus a considerably higher input impedance—about 100 Mohm—is required of the amplifiers to prevent the attenuation and distortion of the myoelectric signal from exceeding permissible values (*Geddes Baker & McGoodwin* 1967) These high impedances may evoke interferences from the surroundings (*Dorcas Libbey & Scott* 1966) Impedance differences of the two signal electrodes may cause the amplifier to be charged with disturbing signals if its input impedance is not sufficiently high Small movements between the skin electrode and the electrolytic layer may cause disturbances in the form of polarization potentials This effect is particularly pronounced in the case of the formerly frequently used stainless steel electrodes (*Lyllen* 1959) Chloridized silver electrodes and a paste containing chloride ions which permit ionic equilibrium give a stable impedance and reduces the motion artefacts (*Day & Lippitt* 1964 *Geddes & Baker* 1967 *Lucels* 1967) A method of reducing motion induced potential disturbances is to arrange a stable fixation between the electrode and the skin by means of a special paste container (*Boter den Hertog & Kuiper* 1966) The motion artefacts can also be eliminated by a conductive polymer bridge between the skin and the electrode (*Thompson & Patterson* 1963) One way of reducing the impedance between the tissue and the electrode—with a less disturbed signal as a result—is besides using electrolytic paste to rub the horny layer of the skin with sand paper (*Nightingale* 1959) However this is impossible if the electrodes are used daily in a prosthesis system The electrolytic paste used with wet electrodes may cause problems due to allergic and toxic skin reactions It is not probable as *Bottomley* (1965) has pointed out that the skin of the amputation stump could stand this for any length of time Another problem connected with skin electrodes is that they pick up signals from a rather large area and thus activity from neighbouring muscles also It has been stated that when two antagonistic muscles are utilized for separate control functions signals produced by one of the muscles should also be picked up by the electrode belonging to the other muscle (*Scott* 1967) resulting in so-called cross talk (*Bottomley et al* 1963) It has been a subject

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of discussion whether this cross talk actually does or does not consist of simultaneous interference activity of the antagonist

In clinical electromyography needle electrodes of various types are routinely used to derive the myoelectric signal intramuscularly The use of these electrodes may cause some discomfort and a risk of infection may arise when they are applied during long periods For these reasons needle electrodes cannot be used in prosthetic control A thin wire percutaneously run into the muscle is a new type of electrode which has many advantages (*Scott* 1965 *Caldwell* 1967) Several methods of inserting these wire electrodes securely have been reported (*Scott* 1965 *Parker* 1968) Problems due to the segregating properties of the skin thus become eliminated but on the other hand activity only from a limited number of motor units in the muscle will be picked up The range of muscle contraction available for recording will thus be reduced (*Bigland* & *Lippold* 1954) Another problem is the measures which regularly must be taken to prevent infection at the site of puncture still another is breakage of the wires These problems were discussed by *Scott* (1966) who also suggested methods of reducing the complications The helical percutaneous electrode designed by *Caldwell* (1967) reduces the risk of wire breakage This electrode offers the possibility of a more stable position as compared to other electrodes in recording how patients can learn by training to control single motor units in a muscle (*Hagman* & *Pierce* 1966 *Caldwell* 1967) It has been stated that this type of training will provide amputees and disabled patients with greater possibilities of myoelectric control and thus render more sophisticated prostheses and orthoses feasible (*Basmajian* 1967)

In so called implant biotelemetry biologic information from a part inside a living organism is wirelessly transmitted to the outside Since 1954 when the transistor became commercially available and the development of microelectronics rapidly advanced biotelemetry has become an important tool in biological studies (*Caceres* *Cooper* & *Mackay* 1965) Implantable electrodes for the telemetry of myoelectric signals through the skin—by means of a frequency modulated wave detected by an external receiver—have been developed (*Ko* 1964 *Hirsch* *Kaiser* & *Petersen* 1966) The main difference between these units is that *Ko* uses batteries as the source of energy whereas *Hirsch et al* utilize externally generated inductive energy Batteries have the drawbacks of being difficult to miniaturize and having short life They must be exchanged at regular intervals which involve the disadvantage of repeated surgery It has been stated however that an implanted battery can be inductively generated This method allows a life of up to three years in a prosthesis system (*Todotnik* & *Greene* 1967) Important demands on an implanted electrode are tissue compatibility stability and capability of providing reproducible signals It should also be possible to sterilize and miniaturize the

electrode to such an extent that it will not affect the normal function of the muscle (*Ko & Neuman* 1967) Initial experiments on animals revealed that a capsule of varying thickness was formed around the implant and that infections and implant flating could result (*Grot Long Ion & Ko* 1965) At the first implantations on man (*Hirsch Kaiser & Petersen* 1966) myo electric signals containing more high frequency activity than those picked up with skin electrodes were obtained The advantages of this type of signal had been stated previously (*Hirsch Kaiser & Petersen* 1964) The advantages of implanted electrodes as compared to other electrodes may result in isolated muscle activity with reduced cross talk or interference a more favourable signal to noise ratio and a broader signal power spectrum Recently several implantable electrodes for the telemetry of myoelectric signals have been designed Implantation experiments primarily on animals are planned (*Peilly* 1968) and some results have already been published (*Scott et al* 1968 *Tucker & Scott* 1968)

The Information Content of Myoelectric Signals

As mentioned before myoelectric prostheses or orthoses can be operated in two ways by on off or threshold control and by proportional control The latter method requires that the salient signal parameter is reproducible and does not become affected by fatigue or artefacts *Scott* (1966) inter alia discussed which property of the myoelectric signal should be selected to control the external system The signal parameter chosen should be easy to utilize by the patient As muscle tension can be controlled voluntarily it was natural to seek a parameter direct correlated to the developed muscle tension

Irrespective of the choice of electrodes the myoelectric signal appearing at moderate levels of contraction reveals a complex pattern in which each motor unit is responsible for certain repeated activities The character of the myo electric signal accordingly is quite irregular and can only be described statistically (*Basmajian* 1967) Consequently several problems are involved if a single parameter of the myoelectric pattern related to total muscle tension is to be utilized for proportional control Two separate parameters reveal the degree of muscle tension viz the amplitude of the myoelectric signal and the firing frequency of the individual units The most common description of a myoelectric signal so far has been to state the so called integrated mean value or root mean square (r m s) value of the amplitude This value is obtained by amplifying rectifying and filtering the myoelectric signal This signal processing is considered to yield a linear relation between signal amplitude and muscle tension in isometric contraction up to the maximum level of contraction (*Lippold* 1952 *Lenman* 1959) It has been discussed whether the

relation is linear at very small and high loads (*Nightingale* 1960) A large time constant of the filter will give a more even relation between the signal amplitude and the muscle tension On the other hand in a myoelectric prosthesis system with feed back a large time constant will cause undesirable oscillations in the prosthesis (*Bottomley Kinnier Wilson & Nightingale* 1963) The time constant must be selected so that the delay introduced into the system will not seriously affect the patient s ability to control the prosthesis (*Bottomley & Cowell* 1964) The relation between integrated signal amplitude and muscle tension in the upper extremities is not quite linear according to these authors However they consider this to be of no importance when the signal amplitude is utilized as a control parameter

In isotonic contractions the constant ratio between r m s signal activity and tension is dependent on both the length of the muscle and the speed at which the muscle length changes as well as the direction of the change (*Bigland & Lippold* 1954) At constant speed the muscle tension increases linearly with the signal activity which in turn is more pronounced in a shortening than a lengthening of the muscle In constant tension there is a linear relation between the signal activity and the speed in the shortening of the muscle but not in its lengthening Muscle tension speed and signal activity are thus related to each other A difficulty arising when stump muscles in amputees are to be used as control sites is that these muscles are not distally anchored The muscles will thus be unloaded during contraction and the speed cannot be assessed (*Alter* 1966)

When muscle contraction increases more motor units become activated and the single unit fires at a gradually higher frequency (*Basmajian Baeza & Fabrigar* 1965) The myoelectric signal can thus be described by measuring the frequency of the motor unit potential spikes in the signal pattern There is also a relation between the frequency of spikes and the muscle tension (*Close Nickel & Todd* 1960) The r m s signal amplitude is proportional to the square root of the frequency of spikes (*Basmajian* 1967) as long as fatigue or synchronization of motor unit potentials do not appear (*Bergstrom* 1959) The calculation of spikes has successfully been tried on normal subjects and *Scott* (1966) considered spike frequency to be a suitable control parameter in a myoelectric system

In the rectified and filtered myoelectric signal there remain due to the statistical character of the signal variations in the mean value of the amplitude These variations are suitably described as a disturbing noise At low levels of contraction the noise is low but it increases gradually with the mean value of the signal amplitude However the amplitude increases more rapidly with the result that the signal to noise ratio increases with an increased level of contraction Not only the myoelectric signal but also back ground noise

which depends on several factors is picked up Tissues and electrodes cause noise contributions the magnitudes of which depend on the respective imped ances There are also polarization potentials and motion induced potentials between the electrode and the skin (*Nightingale* 1959) Frequency analysis of this complex noise has proved it to be mainly confined to low frequencies (*Nightingale* 1959 *Hayes* 1960)

When the amplitude of the myoelectric signal is to be used as a proportional control parameter it is necessary to determine the number of clearly repro ducible signal levels which can be activated irrespectively of each other (*Lodomik & Kreifeldt* 1967) The number of levels depends on the level of contraction as discussed above and on the filtering of the myoelectric signals At a very early stage it was pointed out that myoelectric signals for prosthesis control had to be filtered in order to reduce the disturbances caused by noise from electrodes and amplifiers (*Battye Nightingale & Whillis* 1955) These authors suggested 100–1000 Hz as a suitable range of frequency for the control signal This range was later also recommended by *Horn* (1963) Below 100 Hz the background noise is too loud to be accepted As the signal power spectrum decreases at higher frequencies deteriorating the signal to noise ratio the upper frequency limit in filtering the myoelectric signal was later reduced to 800 Hz by *Bottomley Kinnier Wilson & Nightingale* (1963) The frequency range 300–1000 Hz has also been recommended with the object of excluding the fluctuations of the myoelectric signal believed to exist within the lower frequency ranges (*Hirsch Kaiser & Petersén* 1964) Further knowledge is required to arrive at final recommendations on how myoelectric signals should be filtered Thus it is necessary to learn the relation between developed mechanical force and various parts of the myoelectric signal spectrum

Essentially our knowledge about the information content of the myoelectric signal is based upon normal subjects In amputees and in patients with neurol ogical disturbances there are deviations from the normal physiology which may be very important as has been pointed out by *Wagman* (1966) Thus there may be deviations in the nervous conduction rate in the appearance of motor unit potentials in the power spectra—static and dynamic—and in the effects of temperature deviations also

SCOPE OF THE INVESTIGATIONS

The purpose of the present investigation has been to characterize myoelectric signals in order to create a basis for their utilization in prosthesis control Myoelectric signals were analysed by employing previously introduced methods and methods especially developed for this purpose These studies included clinical examination, conventional EMG analysis of myoelectric power spectra and analysis of the muscle control ability Furthermore, various types of electrodes were studied The attempt was to obtain a detailed characterization of myoelectric signals in normal and arm amputated males The characteristics of the myoelectric signal thus obtained would increase the possibilities of optimizing the signal by suitable filtration

1 In the stump muscles and the proximally situated muscles of arm and leg amputees there are frequently pathological changes in the appearance of the myoelectric signal as determined by conventional EMG (*Blom & Hagbarth* 1964 *Petersén* 1966) It was therefore necessary to carry out further studies on the appearance of the signals in a series of amputees

2 The myoelectric signal must be filtered to obtain an undisturbed myoelectric prosthesis control a fact pointed out earlier in the review of literature Information of the shape of the myoelectric power spectra must be available for all the different muscles in normals and arm amputee

3 Dynamic changes of the spectrum in fatiguing isometric muscle contractions were studied previously in normals (*Kadefors Kaiser & Petersén* 1968) but must also be determined in arm amputees

4 The relative properties of three different types of skin electrode needle electrodes and a refined type of implantable electrode were studied

5 Physiological deviations for instance in speed and precision must be borne in mind when a muscle is intended to be used as a control site in prosthesis control Furthermore, the question arises whether an arm amputee will be able to use his stump muscle in performing rapid and well quantified muscle contractions This ability may depend on whether the remaining muscles are normal or pathological according to the EMG findings On the basis of these series of questions an analysis of the muscle control ability was performed both on normal and arm amputated males by estimating their skill in manoeuvering an electro mechanical apparatus by myoelectric signals

METHODS

Electromyographic Methods

The electromyographic investigations were carried out by means of a 3 channelled DISA Electromyograph (Type 13 A 69). For the tests coaxial needle electrodes (DISA Elektronik 13 K 03) and skin electrodes (DISA Elektronik 13 K 62) were employed. The external diameter of the needle electrode is 0.65 mm and the surface of the internal platinum conductor at the tip is 0.07 mm². The external cannula of the needle electrode is made of stainless steel and well insulated from the internal thin platinum conductor. The skin electrodes are round metal plates (ϕ 7.5 mm) situated at a distance of 23 mm between the centre of each metal plate. The plates are covered with felt and at the examination the felt is moistened with electrolytical paste (Elema Schonander Mingograph Electrode Liquid).

The muscles were first examined in a totally relaxed resting position, then at slight voluntary contraction and finally at the maximum degree of contraction. The needle electrodes were inserted perpendicularly to the direction of the muscle fibres and in view of the existing anatomical variations they were placed at random in four different positions of each muscle at a depth of 0.5–2 cm. The individual motor unit potentials were studied on the screen of the oscilloscope using a sweeping speed of 1 mm/ms. In studying the motor unit potentials suitable amplifications were used, the deflection sensitivity was adjusted to values of 10 µV/mm and in extreme cases it was 1000 µV/mm. Film recording of myoelectric signals was performed at a film speed of 5 cm/s.

It would have been desirable to measure the duration of the single motor unit potential as this parameter is the most valuable in electromyographic diagnostics. However, in several cases it was impossible to collect a sufficiently large number of single and well defined motor unit potentials which covered the requirements of duration measurements (*Buchthal & Clemmesen* 1941, *Petersén & Kugelberg* 1949, *Buchthal, Guld & Rosenfalck* 1954). The reasons were that the remaining muscles in arm amputees often are very small and the patients sensitive to pricks and also that the skin in this area may be very thin and atrophic. According to the conventional clinical electromyographic method of examination both duration and amplitude as well as the number of phases of the individual motor unit potentials were assessed with the naked eye on the screen of the oscilloscope.

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tensor muscles of the forearm The temperature measurements were performed by means of the same thermo couple as mentioned before (FLLAB Type TE_3)

The power spectra were measured by means of a method and an instrument described by *Kaiser & Petersén* (1963 1965) The method is based on transmission of the myoelectric signal through four octave bandpass filters centered at 50 Hz 200 Hz 800 Hz and 1600 Hz respectively The four filter outputs are rectified and the resulting DC voltages are presented using the voltage from the 200 Hz filter as a reference The three ratios obtained—power in the 200 Hz octave over power in the 50 Hz octave power in the 200 Hz octave over power in the 800 Hz octave and power in the 200 Hz octave over power in the 1600 Hz octave—provide a measure of the shape of the power spectrum

The muscle action potentials are first amplified in a DISA Electromyograph the output of which is fed to a specially designed spectrum analyzer The output voltages are presented as the positions of two bright spots the octave loci on the screen of an oscilloscope The horizontal deflections of the two spots are proportional to the 200 Hz/800 Hz and 200 Hz/1600 Hz activity ratios respectively The vertical deflections of both spots are proportional to the 200 Hz/50 Hz activity ratio (Fig 1) All three deflection sensitivities were 1 mm/dB

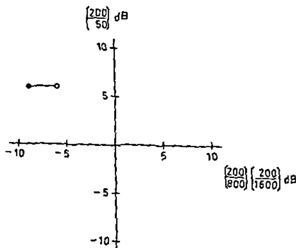


Fig 1 Loci diagram The vertical deflections of both spots are proportional to the ratio in dB of the activity (r m s values) in the 200 Hz band to the activity in the 50 Hz band The horizontal deflections are proportional to the ratio of the activities in the 200 Hz band and the 800 Hz band (circle) and to the ratio of the activities in the 200 Hz band and the 1600 Hz band (filled dot) respectively The loci points in the figure pertain to the case of white noise

The duration and number of phases of the individual potentials are affected by the intramuscular temperature which was measured in a stump muscle of 30 arm amputees In below elbow amputees the temperature was measured in the remaining extensor muscle of the forearm in above elbow amputees in the remaining brachial biceps muscle These measurements were taken with a thermo couple needle from ELLAB Copenhagen (Type TE_3) The needle has a diameter of 0 7 mm and is inserted into the centre of the muscle The temperature was checked at the end of the examinations

Power Spectra of Myoelectric Signals, Methods (Paper I)

Measurements of the myoelectric signal power spectra were performed on 50 healthy males aged from 20 to 50 years and on 30 amputated males of corresponding ages To be included in the series it was necessary that the arm amputees were able to activate myoelectric signals up to a certain level The myoelectric signals were picked up by means of coaxial needle electrodes In cases of uninjured controls signals from eight positions of the needle in nine muscles of the right hand side extremities were analysed

The following muscles were examined in succession mm biceps brachii brachioradialis extensor digitorum communis deltoideus trapezius vastus lateralis tibialis anterior gastrocnemius and soleus

The positions of the needle in the brachial biceps muscle were carefully defined in accordance with a procedure developed by *Kaiser & Petersen* (1965) The needle positions in the other muscles were not defined with this great accuracy Still the needles were placed according to a consistent plan In addition to the nine muscles mentioned above five other muscles were investigated In 25 controls mm biceps brachii brachioradialis and extensor digitorum communis of the left side were examined In all 50 controls four measurements were taken from the left side and four measurements from the right side of mm interosseus dorsalis I manus and extensor digitorum brevis Needle positions in the latter two muscles were not selected to form any particular pattern

In the case of arm amputees myoelectric signals from each muscle investigated were analysed for four needle positions only as the stump region frequently is sensitive to pain and trauma Due to anatomical variations between the arm amputees the needle positions could not be standardized

In the cases of uninjured controls the temperature of the right brachial biceps muscle was measured in the endplate zone of the long head For 20 of the controls the muscle temperature was measured in two definite points on the right side and in an endplate zone of the left side The muscle temperature of the below elbow amputees was measured in the remaining ex

muscle only could be studied In two above elbow amputees and one below elbow amputee adequate myoelectric signals could not be picked up from the brachial biceps muscle Where no signals were picked up the reason was either a lacking muscle or insufficient signal to noise ratio

In accordance with the investigation on normal subjects performed by *Kadefors Kaiser & Petersen* (1968) the purpose of this study on arm amputees was to measure quantitatively spectral changes within high frequency ranges during strong isometric muscle contraction and to measure the recovery rate of these changes

A standard procedure was used for the examinations Initially the patient performed two short forceful muscle contractions followed by an isometric muscle contraction—to the best of his ability—during 30 seconds and immediately afterwards two short contractions After 30 seconds two short contractions were repeated and after a further 30 seconds two short contractions and so on The recovery of the reduced signal amplitude within high frequency ranges which occurred during the persisting contraction was studied during at least 90 seconds The standard schedule is illustrated by Figure 2 showing the signal amplitudes of two octave bandpass filters In the following the designation $D_k = (S_{63} - S_{1000})_k$ expresses the difference in dB of the signal amplitudes for the octave band centered at 63 Hz and the octave band centered at 1000 Hz at a time indicated by k The magnitude $S_{63} - S_{1000}$ was calculated for the moments indicated with arrows in Figure 2 Obviously the reduced magnitude of the signal activity within high frequency ranges can be calculated as $D_5 - D_{1,2,3}$ where $D_{1,2,3}$ is the mean of D_1 and D_2 and D_3 The recovery of the reduced magnitude of activity which occurred within high frequency ranges at different moments (k) is expressed by $D_5 - D_{k,k+1}$

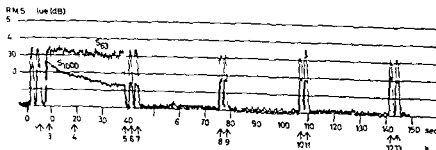


Fig. Th ... gr... showing activity (r.m.s. value) in the 63 Hz band and the 1000 Hz band during a maxim... contraction ($k=3$ ...) followed by a relaxation ... The ... is studied from the analysis of brief contractions ($k-6$ ...) and ... state ($k-1$ ... 3) From *Kadefors Kaiser & Petersen* (1968) by permission

The degree of muscle contraction was standardized with the aid of the contraction level indicator The subjects were instructed to maintain for a few seconds the (moderate) contraction intensity yielding a specified voltmeter deflection During this period the loci coordinates were read—by the same person throughout the entire test series—from the screen of the oscilloscope

In order to give a simple description of power spectrum shape in the standard terms of filter and circuit theory the *three power ratios were transformed* into three new variables These approximate the spectra by a constant level and a straight line the high frequency asymptote which intersects the *constant level at the so called* corner frequency The three transformed spectrum parameters are low frequency level (*is* 200 Hz level) high frequency asymptote slope and corner frequency The statistical analyses were performed for both pairs of three parameters

A detailed analysis of the measurement procedure indicates that the overall systematic error of the power spectrum values obtained is less than 1 dB For further details of the procedure employed in describing the shape of the power spectrum and the statistical analysis involved see Paper I

Dynamic Spectrum Analysis, Method and Instrumentation

Dynamic changes in the power spectrum of the myoelectric signal in a fatiguing isometric muscle contraction were analysed in different octave band pass filters by means of a broad band frequency analyzer (*Bruel & Kjaer* Type 2112) according to the method used by *Kadefors Kaiser & Petersen* (1968) Following the notation of these authors the symbol S_f was used for the signal power expressed in dB within an octave band with a centre frequency of f Hz The myoelectric signals were amplified in a DISA Electromyograph and then recorded on magnetic tape (Precision Instrument PI 200) The analysis of the spectrum was performed from the recorder The different octave bandpass filters were switched in one by one *and the signal amplitude* (r m s)—expressed in dB—was written by means of a level recorder (*Bruel & Kjaer* Type 2305) The error of the entire analysis was within ± 1.5 dB

Needle electrodes of the same type as earlier were used for picking up the myoelectric signals and signals from several muscles were recorded for all but two *of the 30 arm amputees Among the below* elbow amputees muscles on the extensor side of the forearm (closely corresponding to m extensor digitorum communis) could be studied in 19 cases this also applied to the brachioradial muscle *The remaining stump flexor muscles were studied in 12 cases* In 27 of the 30 arm amputees the brachial biceps muscle was examined Five of these patients had been above elbow amputated and thus the remaining part of the

mu ck onl could be studied In two above elbow amputees and one below elbow amputee adequate myoelectric signals could not be picked up from the brachial biceps muscle Where no signals were picked up the reason was either a lacking muscle or insufficient signal to noise ratio

In accordance with the investigation on normal subjects performed by *Kadefors* Kaiser & Petersen (1968) the purpose of this study on arm amputees was to measure quantitatively spectral changes within high frequency ranges during strong isometric muscle contraction and to measure the recovery rate of these changes

A standard procedure was used for the examinations Initially the patient performed two short forceful muscle contractions followed by an isometric muscle contraction—to the best of his ability—during 30 seconds and immediately afterwards two short contractions After 30 seconds two short contractions were repeated and after a further 30 seconds two short contractions and so on The recovery of the reduced signal amplitude within high frequency ranges which occurred during the persisting contraction was studied during at least 90 seconds The standard schedule is illustrated by Figure 2 showing the signal amplitudes of two octave bandpass filters In the following the designation $D_k = (S_{63} - S_{1000})_k$ expresses the difference in dB of the signal amplitudes for the octave band centered at 63 Hz and the octave band centered at 1000 Hz at a time indicated by k The magnitude $S_{63} - S_{1000}$ was calculated for the moments indicated with arrows in Figure 2 Obviously the reduced magnitude of the signal activity within high frequency ranges can be calculated as $D_5 - D_{1,2,3}$ where $D_{1,2,3}$ is the mean of D_1 and D_2 and D_3 The recovery of the reduced magnitude of activity which occurred within high frequency ranges at different moments (k) is expressed by $D_5 - D_{k,k+1}$

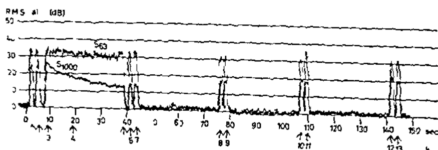


Fig. The standard programme showing activity (r.m.s. value) in the 63 Hz band and the 1000 Hz band during a maximum contraction ($k=3$) followed by a relaxation. The recovery is studied from the analysis of brief contractions (k ...) and compared to the initial state ($k = 1$ ... 3). From Kadefors, Kaiser & Petersen (1968) by permission

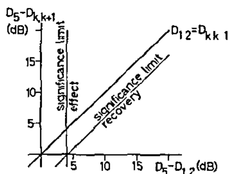


Fig 3 Diagram showing the effect and recovery phenomena in a maximum muscle contraction The abscissa shows increase in difference between the 63 Hz and the 1000 Hz components in dB The ordinate shows the recovery state at a particular time instant From *Kadefors Kaiser & Petersén* (1968) by permission

where $D_{k,k+1}$ is the mean of D_k and D_{k+1} It is easier to explain this condition by a diagram (Fig 3) In this figure a value on an abscissa of 4 dB or less means that there is no significant reduction of the high frequency components This value was obtained by calculating the statistical properties of the signal and by considering the error of method (*Kadefors Kaiser & Petersen* 1968) The figure also illustrates that if the distance between a measured value and the line $D_5-D_{1,2}=D_5-D_{k,k+1}$ exceeds 4 dB the recovery is not considered to be significant The encircled point in the figure indicates a muscle contraction where the effect regarding the decay of high frequency components is significant but the recovery is not complete

The values obtained from the amputees have been compared with the normal values stated by *Kadefors Kaiser & Petersén* (1968) No mention is made as to which side was tested at the investigation but according to personal communication with the authors all the signals were picked up on the right hand side The purpose of the present investigation was to study the dynamic changes in the spectrum of myoelectric signals obtained from amputees in connection with fatiguing muscle contractions Due to the limited number of observations of each muscle the series was not divided into left and right hand sides nor into levels of amputation A comparison with the normal series is despite this of importance as for practical reasons it is valuable to know any deviating dynamic changes of the spectrum in amputees before performing signal processing Differences in muscle effect and recovery between normals and amputees were analysed by the ordinary T test

Methods of Comparing Electrodes (Papers II, III)

Several methods have been used for comparison of the properties between different types of electrodes In three commercially available surface electrodes for protheses (Austrian Viennatone Italian INAIL and the Russian) the impedance was measured as a function of frequency The impedances of the electrodes were calculated by means of the voltage drop at a constant current

of 10 µA measured with the aid of a phase sensitive voltmeter (Solartron VP 250) All the recordings were performed with the electrode in a standardized position on the extensor side of the forearm The ground electrode was placed on the flexor side and consisted of a large wet silver plate

By means of a voltmeter (HP 425 A) differences between the half cell potentials of the electrodes were measured These measurements were also performed in a standardized position on the extensor side of the forearm Before the recordings the skin was carefully cleaned with alcohol and each type of electrode was tested ten times

A comparison of the signal to noise ratio in dB between the different electrodes could be obtained by measurements performed on similarly placed electrodes on the forearm and at accurately controlled muscle contractions By loading the finger extensors of the forearm with a constant rather small weight (1 kg) a comparable degree of contraction was obtained As an amplifier a DISA Electromyograph was used and the 250 Hz octave band was selected for the analysis giving the best signal to noise ratio The noise level was measured at complete relaxation and was reproducible to within 2–3 dB

Some spectral characteristics obtained in the signal to noise ratio investigation were compared between the surface electrodes and an implanted electrode The analysis was performed on an octave band analyzer (*Bruel & Kjaer* 2112)

Six electrodes for telemetry of the myoelectric signals were implanted on four voluntary subjects two uninjured controls and two below elbow amputees The operations were performed under local anaesthesia and the electrodes were placed subcutaneously above the fascia A technical description of the electrode is given in Paper III The subjects were observed clinically and the tissue reaction after removal of the electrodes was studied macro and microscopically The following methods for analysis of the recorded signals were used study via rectification and integration of the total signal spectral analysis and study via graphic recording In the present study analysis has been undertaken by using a tape recording velocity of eight times the play back velocity All frequencies were thus divided by eight A conventional ink jet recorder (ELEMA Schonander Mingograph 42) capable of writing frequencies up to some hundreds of Hz is adequate Rectification and integration of the total signal and spectral analysis were performed with the same analyzer as used before (*Bruel & Kjaer* 2112) Furthermore spectral analysis was performed with the apparatus described by *Kaiser & Petersén* (1963 1965)

Control Ability Test Apparatus and Procedure (Paper IV)

When a muscle is utilized as a control site for prosthesis control the fact that anatomical and physiological conditions differ between various muscles is of

importance The distal extremity muscles often have a larger degree of innervation (*Feinstein, Lindegard Nyman & Wohlfart* 1955) and thus their control is more appropriate as compared to proximal muscles This is believed to cause differences in speed and fatiguability (*Tergast* 1873) The aim of this investigation was not to study the speed and dynamics of separate muscles in order to characterize a control site The purpose was to get an idea of the ability to manoeuver a specially designed electro mechanical test instrument using myoelectric signals This yielded knowledge of the ability of uninjured and arm amputated males *to perform rapid and voluntary quantified muscle* contractions

In a preliminary investigation three muscles in 30 uninjured males aged between 20 and 50 years, were studied the mm extensor carpi radialis longus deltoideus and vastus lateralis (Paper IV) Based on the experience of this investigation the instruction of the test subjects was modified at the definite investigation Thus a further series of 30 uninjured males—in the same age groups—was tested The nine muscles included in the definite investigation were mm extensor carpi radialis flexor digitorum sublimis interosseus dorsalis I manus biceps brachii triceps deltoideus trapezius *vastus lateralis tibialis anterior All these tests were performed on the right* hand side

In 30 arm amputees with varying levels of amputation a number of muscles were studied the stump muscle on the extensor and flexor sides of the fore arm mm biceps brachii and deltoideus The amputations were performed on the right hand side in 13 cases The method does not permit any differentiation of the manoeuverability between the right and left hand sides Consequently there was no distinction made between the right and left hand sides in the amputation series

Surface electrodes (DISA Elektronik 13 K 62) picked up the myoelectric signals which were amplified in a DISA Electromyograph before being connected to one of the inputs of the test instrument A signal from a test programme—recorded on tape—was connected to the other input The actual test instrument is electro mechanical and the technical description of this and of the test programme is described in Paper IV

Apparatus and Test Programme

The two input signals the myoelectric signal and the programme signal are rectified and converted to pulses of a frequency proportional to the level of the input signals The output pulses are connected to a stepping motor which runs forwards and backwards *depending on which input signal has the highest* amplitude In the mechanical system the stepped motor activates a tiltable

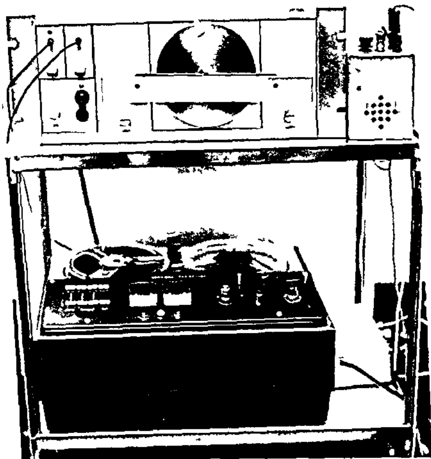


Fig 4 The electromechanical apparatus with its frame and fly wheel as the test subject will experience the system during the course of examination. Below a tape recorder and the standard programme

frame which moves freely around a horizontal axis having moving increments of 1 7 milliradians per pulse constituting the so called primary movement A cylindrical shaft is placed on the frame and when the frame tilts the shaft rotates thus causing the secondary movement On the front end of the cylindrical shaft which protrudes through an aperture in the face plate of the apparatus there is a fly wheel with an outer diameter of 14 cm The rate of angular acceleration of this wheel is 8 milliradians/sec² per milliradian tilt of the frame A mark on the wheel indicates the centre of the system (Fig 4)

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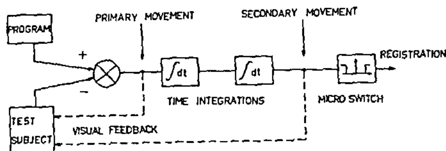


Fig 6 Block diagram showing the function of the electro mechanical apparatus in principle The interaction between the deviation of the frame and the angular deviation from the centre position of the fly wheel can be expressed as two successive time integrations There are two visual feed backs the deviations of the frame and the fly wheel respectively

jects were instructed about the purpose of the examination the function of the instrument and the test procedure They were then requested to try to maintain the frame in a horizontal position and the fly wheel in the centre by alternating activation and relaxation of the muscle to be tested However there are two differences in the methods of the preliminary (Paper IV) and the definite investigations In the first place it was especially emphasized that the subjects should concentrate on the tilt of the frame and only in extreme positions should they pay attention to the fly wheel Secondly the subjects rested comfortably with their arms on a support at the definite investigation of the deltoid muscle As a matter of fact it proved difficult to relax the deltoid muscle with the arm hanging as at the previous test

The function measured by this apparatus is of course extremely complex The relation between man and machine according to the above test is approximately illustrated in a block diagram (Fig 6) The comparatively uncomplicated test programme resulted in the subjects satisfactory control of the apparatus during the greater part of the test The fly wheel deviated considerably from the centre during short periods only The secondary movement i e the position of the wheel is characterized by an approximately normal distribution and the instability of the position of the wheel is best described by the standard deviation To designate this complex function of the apparatus the term manoeuverability was introduced

A study of the manoeuverability of various muscles in both uninjured subjects and amputees was considered justified in view of the future prosthesis applications The following questions arose at the definite investigation

1 Does the ability to manoeuver the apparatus myoelectrically differ between various arm muscles in healthy males?

At a certain adjustable angular deflection of the wheel, a micro switch is activated and its position is recorded continuously (ELEMA Schönander Mingograph 42) The error is chosen so that the error indicating switch is activated if the wheel deviates more than $\pm 90°$ from the centre The accumulated time the so called off time during which the position of the wheel lies outside the error limits is indicated on the recorder

The test programme was tape recorded from a laboratory oscillator For each test on each muscle the total time required was 260 seconds The programme signal is connected to a loud speaker one input of the apparatus and the recorder To neutralize the great importance of the factor of adaptation the subjects were both at the preliminary and at the definite tests initially examined twice utilizing the same muscle The difficulty factors of the test programme and the amplification of the DISA—apparatus were selected in a way which obviously permitted all the subjects to grasp quickly the principle of the programme and fulfil it with minor errors In all the subjects the muscles were tested in sequences

During the tests the subjects were comfortably seated in an adjustable chair *with the possibility of relaxing completely (Fig 5) A carefully elaborated* standard procedure was followed at each examination To begin with the sub

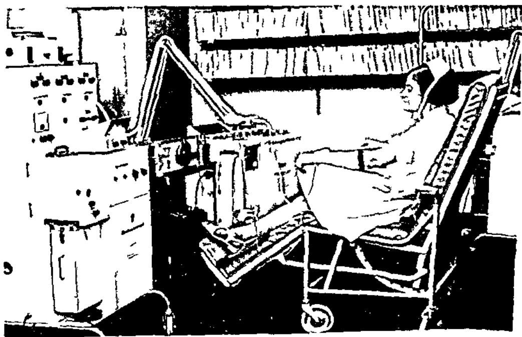


Fig 5 A test subject sitting comfortably in front of the apparatus during the course of the manoeuvering test To the left the DISA Electromyograph and to the right of the apparatus the recorder Surface electrodes are used to pick up the myoelectric signal

MATERIAL

The series included 30 males who had been arm amputated during the period 1934–1966 With the exception of five patients resident in Stockholm they all belonged to the Gothenburg area and received their prostheses at the Orthopaedic Clinic in Gothenburg Males of ages ranging from 20 to 50 years were selected as the males in the control groups were of corresponding ages No patients with congenital defects were included As the purpose was to study changes in stump muscles following amputation only above and below elbow amputees were examined No patients with fore quarter resec tions were included In the series available no patients had exarticulations either in their wrists or their elbow joints One bilateral arm amputee was included As the deficiency in this patient was congenital on one side only the operated arm was examined

Table 3 Level of amputat on related to age

Ag at examination	Above elbow	Below elbow	Total
0–		4	4
6–30	1	5	6
31–3			
36–40	1	1	[illegible]
41–4	3		8
46– 0	[illegible]	8	10
Total		23	30

The series consi ted of seven above elbow amputees and 23 below elbow amputees and the di tribution of the levels of amputation in the various age groups is tabulated (Table 3) One third of the patients were aged between 20 and 30 years and one third between 45 and 50 years and the remaining patients were di tributed between the two first age groups As most of the patients were operated upon at hospitals in different parts of Sweden and abroad many years ago information about the technique used at the opera tion was in few cases only available

The patient s age at the time of amputation and the number of years elapsed since can be studied in Table 4 Most of the patients were operated on between

2 If such a difference exists is it correlated to the proximal muscles as compared to the distal muscles?

3 Does the ability to manoeuver the apparatus differ with respect to the remaining muscles in arm amputees being normal or showing a peripheral neuron lesion according to conventional electromyography?

4 Does the ability to manoeuver the apparatus differ between healthy and arm amputated males with corresponding muscles?

Statistical Analysis

The statistical methods used to evaluate the results from this investigation were designed separately for each of the questions at issue

The off times for the nine muscles of normal males were analysed by means of a two way analysis of variance mixed model where the muscles were considered as a fixed effect and individuals as a random effect No replicates were made which means that the interaction cannot be tested For physiological reasons however it can be assumed that the interaction effect is negligible In order to fulfil the conditions of the analysis of variance it was performed on the natural logarithms of the off times When the analysis of variance showed significant main effects Scheffe s S method was employed to compare individual contrasts

The difference in off times between muscles in arm amputated males showing normal or pathological EMG was analysed statistically using the Wilcoxon Two Sample Rank Test on the original values This method was chosen because of the rather limited number of observations which did not satisfy the conditions of the normal approximation

The difference in off times between muscles in normal and arm amputated males was analysed by the ordinarily normal test on the natural logarithms of the off times

A 5% level of significance was used throughout The statistical analyses employed are described in full detail in Brownlee (1960)

In the remaining group of trauma it is mostly children and adolescents who are the victims for instance in blasting accidents when playing with explosive material In 13 cases the right arm and hand were amputated and in 17 cases the left

Despite long standing handicap most of the patients as a rule have a remaining phantom limb perception of the lost hand (*Cronholm* 1951) In 19 cases this perception did not cause any discomfort but in seven cases pain was experienced which the patient localized to the lost hand (Table 6) Besides this phantom pain four patients experienced a varying degree of pain in the stump Of the patients claiming phantom pain four stated that it was gradually disappearing Three patients mentioned that the actual phantom perception of the lost hand had become reduced In 18 of the 26 patients who had a phantom perception there was a general tendency to perceive the entire hand while the remaining 8 only perceived part of the hand Furthermore five patients claimed that the stump was extremely sensitive to cold

Among the types of prosthesis the passive cosmetic hand predominates and in this series 18 patients use it regularly all day The prostheses have been classified in active functional hand prostheses and hooks as opposed to passive prostheses of different types Table 7 depicts the distribution of the

Table 6 Number of patients with a phantom hand perception in relation to amputation level

Level of amputation	Phantom hand perception: Without pain	With pain	Total
Above elbow	4		6
Below elbow	1		0
Total	19	7	?6

Table 7 Number of different types of prostheses used in relation to amputation level

Level of amputation	Type of prosthesis used: Active hand	Passive hand	Active hook	Passive hook	Passive other type	Total
Above elbow	1			-	1	9
Below elbow	3	13	4		3	8
Total	4	18	4	7	4	3

Table 4 *Age at amputation related to number of years of handicap*

Period of amputation years	Age at amputation –10	11–20	21–30	31–40	41–50	Total
2–5		2	1		1	4
6–10					1	1
11–15	1	2	3	2		8
16–20	3	1	1	[illegible]		7
21–25		2	1			3
26–30		4	1			5
31–35	1		1			2
Total	5	11	8	4	2	30

Table 5 Causes of amputation in relation to age at amputation

Age at amputation	Etiology: Industrial accidents	Traffic accidents	Different trauma	Tumour	Infection	Total
2–10		1	3	1		5
11–15	1		3			4
16–20	2	1	2	1	1	7
21–25	2	1	2			5
26–30	2	1				3
31–35	2					2
36–40	2					2
41–45		1				1
46–50	1					1
Total	12	5	10	[illegible]	1	30

the ages of 11 and 30 years This is in accordance with several earlier publications in which it was stated that arm amputations mainly strike young individuals The number of years during which the patients in this series had been amputated are evenly divided into intervals of five years from one year up to 33 years In half of the series the operation had been performed 10–20 years earlier

Recent investigations show that the most common cause of arm amputations are traumatic injuries As the congenital defects constituting the next largest etiological group of arm amputees were excluded from this series the traumatic causes predominate This is seen in Table 5 in which the causes of amputation and the age of the patients are stated Traumatic injuries occurred in 27 cases tumours in two cases and infection in one case Industrial and traffic accidents strike different age groups more or less at the same rate

In the remaining group of trauma it is mostly children and adolescents who are the victims for instance in blasting accidents when playing with explosive material In 13 cases the right arm and hand were amputated and in 17 cases the left

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Level of amputation	Phantom hand perception: Without pain	With pain	Total
Above elbow	4		[illegible]
Below elbow	1		[illegible]0
Total	19	[illegible]	[illegible]

Table [illegible] Number of different types of prostheses used in relation to amputation level

Level of amputation	Type of prosthesis used: Active hand	Passive hand	Active hook	Passive hook	Passive other type	Total
Above elbow	1	5			1	9
Below elbow	3	13	4	[illegible]	3	8
Total	4	18	4		4	3

prostheses with regard to the level of amputation A combination of two types of prosthesis was used by nine patients A passive hook was exchanged for the cosmetic hand in certain activities One above elbow and one below elbow amputee never used any prosthesis Furthermore there were two patients who only used their prosthesis at work A third of the patients had tried but never learnt to utilize and appreciate an active prosthesis fitted by means of wires Among the seven above elbow amputees, five patients use an actively controlled elbow joint and in addition to this a cosmetic hand These patients could not accept two cables one for elbow flexion and one for prehension The fact that the patients do not utilize their active pro the es may be due to the lack of specialized rehabilitation centres in Sweden for arm amputees Seven patients stated that they are dependent on their pros thesis

In general few arm amputees regularly use their prosthesis However there are great variations in earlier published findings *Muller* (1962) in his follow up of 64 arm amputees found that 29 per cent used their prosthesis regularly *Nathan & Davidoff* (1965) stated that of 36 arm amputees 14 never used their prosthesis In the present series of 30 amputees 25 use their prosthesis every day at work and at home The fact that the series is a selected group in which the patients are of ages below 50 years may explain their using the prosthesi Due to the fact that every patient can receive a prosthesis free of charge in this country a very detailed and individual technical fitting can be made This may al o explain the high frequency of prosthesis carriers

When asked 21 patients stated that they managed independently at work and at home Eight patients required assistance in tying their shoe laces neck ties and in fastening buttons Only one patient mentioned that he re quired help every day with his personal care This patient was above elbow amputated and slightly mentally retarded

Mental disturbances mainly depression and a tendency to isolation are common complaints and two thirds of the patients had similar trouble during the first years after the amputation On the other hand there are only four patients who have remaining mental complications due to their handicap However all the patients have adapted themselves socially except one who is a criminal

As the patients are well taken care of and offered the possibility of learning a new job—at public expense often during several years—their social adapta tion becomes facilitated

RESULTS

Clinical Investigation

All the patients were subjected to the following clinical examination inspection palpation assessment of range of motion and force and testing of sensibility of the stump The range of motion in the shoulder and the elbow joints and the pronation and supination were measured with a goniometer The physical strength of the arm was compared with that of the uninjured side and classified as normal or considerably reduced The sensibility of the stump was tested for pricks and touch and subjected to Weber s two point discrimination test according to the procedure emphasized by *Moberg* (1962 1963 1964) The sense of vibration was examined on all the stumps The length of the amputation stump was measured On the below elbow amputees the length on the dorsal side of the forearm from the tip of the olecranon was measured and likewise from the acromion on the lateral side of the stump in above elbow amputees The lengths of the amputated stumps have varied considerably (Table 8)

T 11 8 Stump l ngth n relat on to amputation l vel

Length of stump cm	Abo e elbow	B low elbow	Total
0			2
€ 10			ↄ
11–1			4
16– 0	-	10	1
1	1	3	4
6–30		1	3
Total		3	30

I ı ȷ cti n

Among the below elbow amputees the stump generally was of a good shape but in six patients the stumps which were short revealed different degrees f deformation i e lengths below 10 cm The patients with long below elbow

stumps nearly all had normal skin and thin short movable scars across the tip of the stump However two of these patients with long below elbow stumps had larger scars in one case consisting of two skin grafts In seven of the below elbow amputees with short stumps more than half of the cases had small areas of adherent thin skin Two of these had excess skin which deformed the stumps and made them soft These patients have had difficulties in getting a satisfactory prosthesis application Only one patient with a short below elbow stump had a symmetrical stump with acceptable skin

At the inspection five of the seven patients subjected to above elbow amputation were found to have considerably deformed stumps The remaining muscles were small and retracted in these five patients and furthermore there were large scars to a great extent adherent to the subjacent bone One of the above elbow amputees had a soft stump with an excess of skin

Already at the inspection the remaining part of the extremity revealed considerable atrophy in several cases In the below elbow amputees atrophy of the upper arm was found in six patients However the shoulder muscles were not affected in these patients Atrophy was present in all the above elbow amputees Among these there were three cases with reduced shoulder muscles mainly including the deltoid muscle and the supraspinate muscle As all the above elbow amputees in this series except for one patient only utilize cosmetic hand prostheses atrophy will often set in due to inactivity

Palpation

Besides the skin also the muscles and the other tissues were examined when palpating the stump As has been pointed out earlier the above elbow amputees had considerably reduced stump muscles and the remaining part of the biceps muscle was retracted in all the cases but one In the below elbow amputees the stump muscles were seldom reduced Among the patients with long below elbow stumps the muscle was reduced only in three cases Retraction of the stump muscle was found in two below elbow amputees

In the below elbow amputees there were three cases of neuroma all originating from the median nerve In the above elbow amputees two neuroma originating from the radial and axillary nerves were found At the palpation all the neuroma were diagnosed due to pain or their considerable size In that connection attempts were made to assess the patient s ability to contract the remaining stump muscles on the extensor and the flexor sides irrespectively of each other Only in one below elbow amputee with an extremely long stump was this ability noticed without earlier training As a whole the patients have clearly experienced their inability to contract the remaining muscles independently of each other and had a sensation of activat

ing the entire stump as a unit The patients who perceive distinctly the opening and closing of their phantom hand no doubt found it easier to try to contract the remaining stump muscles independently

Range of Motion

Three below elbow amputees and five above elbow amputees had impaired mobility of their shoulder joint on the amputated side The rate of below elbow amputees with this impairment is smaller as compared to earlier investigations Thus *Solonen et al* (1965) found impaired mobility of the shoulder joint in 27 per cent of 48 above elbow amputees and in 29 per cent of 24 below elbow amputees This discrepancy is no doubt due to the low mean age of the below elbow amputees in this series while the mean age of Solonen s series of disabled soldiers was 45 years Painful impaired motion of the shoulder joint was found in one patient only The degree of limited motion was slight and in all the patients the range of abduction was at least 160 and the degree of rotation was a minimum of 120

Of the below elbow amputees 15 patients had a normal range of motion of the elbow joint on the amputated side In a third of these patients impaired flexion was observed This was pronounced only in three cases ri between 2 and 75 Hyperextension between 20 and 30 was found in three patients None of the below elbow amputees experienced pain when forcing the movements of the elbow joints which were all stable in an extended position No radiographic examination was performed

The remaining ability to pronate and supinate depended on the length of the stump (Table 9) In the cases where the length of the stump exceeded 15 cm all except two patients could rotate their forearm more than 90

Tabl 9 Range of mo em nt pronat on supinat on at diff rent stump lengths

Length of stump cm	Pro sup nat on			
	–45	4 –90	> 90	Total
0– 5				
6–10	4	1		-
11–1	1	1		-
16–20		4	6	10
> 0			4	4
Total	-	6	10	3

stumps nearly all had normal skin and thin short movable scars across the tip of the stump However two of these patients with long below elbow stumps had larger scars in one case consisting of two skin grafts In seven of the below elbow amputees with short stumps more than half of the cases had small areas of adherent thin skin Two of these had excess skin which deformed the stumps and made them soft These patients have had difficulties in getting a satisfactory prosthesis application Only one patient with a short below elbow stump had a symmetrical stump with acceptable skin

At the inspection five of the seven patients subjected to above elbow amputation were found to have considerably deformed stumps The remaining muscles were small and retracted in these five patients and furthermore there were large scars to a great extent adherent to the subjacent bone One of the above elbow amputees had a soft stump with an excess of skin

Already at the inspection the remaining part of the extremity revealed *considerable atrophy in several cases In the below elbow amputees* atrophy of the upper arm was found in six patients However the shoulder muscles were not affected in these patients Atrophy was present in all the above elbow amputees Among these there were three cases with reduced shoulder muscles mainly including the deltoid muscle and the supraspinate muscle As all the above elbow amputees in this series except for one patient only utilize cosmetic hand prostheses atrophy will often set in due to inactivity

Palpation

Besides the skin also the muscles and the other tissues were examined when palpating the stump As has been pointed out earlier the above elbow amputees had considerably reduced stump muscles and the remaining part of the biceps muscle was retracted in all the cases but one In the below elbow amputees the stump muscles were seldom reduced Among the patients with long below elbow stumps the muscle was reduced only in three cases Retrac*tion of the stump muscle was found in two below elbow amputees*

In the below elbow amputees there were three cases of neuroma all originating from the median nerve In the above elbow amputees two neuroma originating from the radial and axillary nerves were found At the palpation all the neuroma were diagnosed due to pain or their considerable size In that connection attempts were made to assess the patient s ability to contract the remaining stump muscles on the extensor and the flexor sides irrespectively of each other Only in one below elbow amputee with an extremely long stump was this ability noticed without earlier training As a whole the patients have clearly experienced their inability to contract the remaining muscles independently *of each other and had a sensation of activat*

ing the entire stump as a unit The patients who perceive distinctly the opening and closing of their phantom hand no doubt found it easier to try to contract the remaining stump muscles independently

Range of Motion

Three below elbow amputees and five above elbow amputees had impaired mobility of their shoulder joint on the amputated side The rate of below elbow amputees with this impairment is smaller as compared to earlier investigations Thus *Solonen et al* (1965) found impaired mobility of the shoulder joint in 27 per cent of 48 above elbow amputees and in 29 per cent of 24 below elbow amputees This discrepancy is no doubt due to the low mean age of the below elbow amputees in this series while the mean age of Solonen s series of disabled soldiers was 45 years Painful impaired motion of the shoulder joint was found in one patient only The degree of limited motion was light and in all the patients the range of abduction was at least 160 and the degree of rotation was a minimum of 120

Of the below elbow amputees 15 patients had a normal range of motion of the elbow joint on the amputated side In a third of these patients impaired flexion was observed This was pronounced only in three cases i e between 2 and 7 Hyperextension between 20 and 30 was found in three patients None of the below elbow amputees experienced pain when forcing the movements of the elbow joints which were all stable in an extended position No radiographic examination was performed

The remaining ability to pronate and supinate depended on the length of the stump (Table 9) In the cases where the length of the stump exceeded 1 cm all except two patients could rotate their forearm more than 90

Table 9 Range of movement pronation supination at different stump lengths

Length of stump cm	Pro supination			Total
	-4	4–90	> 90	
0–5	-			
6–10	4	1		
11–1	1	1		2
16–0		4	6	10
> 0			4	4
Total	7	6	10	43

Physical Strength

The physical strength in the shoulder muscles of the above elbow amputees was considerably reduced in three patients on the amputated side The others had, despite existing atrophy an almost normal physical strength The force of extension in the elbow joint was considerably reduced in five below elbow amputees The force of flexion of the elbow joint was considerably reduced as compared to the uninjured arm in six patients Furthermore in two patients the force in flexing the elbow joint was extremely reduced The pronation and supination strength was almost intact in half of the patients with long stumps The other below elbow amputees who had a remaining pronation supination ability revealed varying strength which however was difficult to estimate when the stumps were short

Sensibility

In all the patients a tuning fork (C 128) was used to check that the sense of vibration was normal In 12 of the amputees there was reduced sensibility within different areas of the stump In five of the cases the disturbed sensibility for pricks and touch was localized in grafts or large scars All the above elbow amputees except one had impaired sensibility in areas of varying sizes A pathological two point discrimination as compared to the uninjured arm was found in 11 patients In five cases the pathological two point discrimination was also found only within areas of cicatrices or grafts Among the other six patients two point discrimination was measured to range between 30 and 40 mm in two cases In four patients no two point discrimination could be measured in the comparatively small areas involved The size of the skin area where an impaired or a neutralized sensibility was found varied between 5 and 18 cm and was situated within the distal part of the stump

The clinical results are summarized in Table 10 The table shows that below elbow amputees with short stumps on the whole revealed numerous changes The stumps were irregularly shaped the skin was thin often adherent and frequently the sensibility was impaired There was no pronation or supination left and the mobility of the elbow was reduced as the physical strength was impaired as a rule Technically it is always difficult to apply a prosthesis to a short stump Due to the above mentioned reasons the changes among these patients further complicate a satisfactory fitting of the prosthesis In patients with long forearm stumps these changes are only found occasionally However the length of the stump is decisive for the degree of rotation The stumps of the above elbow amputees are all irregular and atrophic often the skin is thin and the sensibility is disturbed Despite this they have

	Flex	Ext	Loss (t n)	(t on)	(xt on)	(flow flex)	(on t n)	(n t on)	(pain)	(two joint)
[illegible]	180	110	0	0		–			–	
4	180	30	0	0					–	–
[illegible]	180	0	10	0		+			+	+
8	10	45	10	10	+	+			–	–
7	00	10	10	10	+	+			+	+
[illegible]	18	40	40	0		–	–	–	+	+
10	180	?0	0	0	+	–			–	–
10	180	40	0	0	–	–			–	+
1	180	3	4	40	+	+	+	+	+	+
4	180	3	60	80	+	–	–	–	+	+
6	?00	3	4	0	+	+	–	–	+	+
8	180	3	30	0	+	+	–	–	+	+
7	180	3	4	1	+	+	–	–	+	+
[illegible]	180	3	70	0	+	+	–	–	+	+
7	180	3	30	10	–	–	–	–	+	+
[illegible]	180	4	0	4	+	+	–	–	–	–
8	180	3	90	60	+	+	+	+	+	+
[illegible]	180	30	80	4	+	+	–	–	+	+
0	180	3		4	+		+	+	+	+
[illegible]	180	3	10	10	+	+	+	+	+	+
[illegible]	180	3	65	30	+	+	+	+	+	+
1	180	40	0	0	+	+	+	+	+	+
[illegible]	180	3	00	30	+	+	+	+	+	+

a remarkably good and painless mobility of the shoulder joint and the physical strength is only reduced moderately.

Electromyographic Results

The electromyographic results are indicated in Table 11. In the above elbow amputees three different muscles were studied and in the below elbow amputees six muscles. In some cases a muscle was excluded from the investigation as the remaining muscle, if any, could not be identified. Pathological changes of the myoelectric signals picked up from stump muscles were found in both above- and below-elbow amputees in 40 per cent of these muscles. *The type of pathological changes in the myoelectric signal appeared* as a peripheral neuron lesion in all cases except one. This patient had a serious infection which resulted in amputation due to gangrene. In the extensor muscle and the brachioradial muscle of the forearm stump there were EMG changes which could be interpreted as myopathy. However, similar changes are found in reinnervation.

In three cases of the above elbow amputees there was a typical peripheral neuron lesion present in the remainders of the biceps muscle and in two cases of the triceps muscle. Among the below elbow amputees there existed a peripheral neuron lesion in the brachial biceps in three cases and in the triceps muscle in two cases. The latter amputees obviously had lesions of the lower

Table 11. EMG findings in different muscles of the amputation side in relation to level of amputation

Investigated muscles	Above elbow				Below elbow			
	Normal EMG	Lower motor neuron lesion	Myopathy or reinnervation	No. of muscles available for exam.	Normal EMG	Lower motor neuron lesion	Myopathy or reinnervation	No. of muscles available for exam.
M. deltoideus	6	1	–	7	23	–	–	23
M. biceps brachii	4	3	–	[illegible]	20	3	–	23
M. triceps	2	–	–	4	21	–	–	23
M. brachioradialis					18	2	1	21
M. extensor digitorum					13	8	1	22
M. flexor digitorum					15	6	–	21
Total	12	6	–	18	110	21	2	133

Table 1. EMG findings in the investigated muscles in relation to amputation level and length of stump. + indicates normal EMG; − lower motoneuron lesion; M myopathy or reinnervation

Level of amputation	Length of stump cm	Stump muscle extensor side of the stump	Stump muscle flexor side of the stump	M. brachioradialis	M. biceps brachii	M. triceps	M. deltoideus
		EMG findings					
	4			+	−	−	+
		−	−	−	+	−	−
	8	+	+	+	+	+	+
	9	−	+	+	+	+	+
	9	−	+	+	+	+	−
	10	M	−	M	+	+	+
	10	−			−	+	−
	1	+	+	+	+	+	−
	14	−	+	+	−	+	+
	16	+	+	+	+	+	+
	16	+	−	+	+	+	+
Below	1	+	+	+	+	+	−
elbow	1	−	+	+	+	+	+
	1	+	+	−	+	+	+
	1	−	−	+	−	+	+
	18	−	+	+	+	+	−
	19	−	+	+	+	+	+
	0	−	+	+	+	+	−
	0	−	−	+	+	+	+
		−	+	+	−	+	−
	4	+	+	+	+	+	+
		+	−	+	+	+	−
	5	−	+	+	+	+	+
	11				−		+
	13				+		+
	17				−	−	+
Above	0				−		−
elbow	4				−	−	+
	6				+	−	+
					+	−	−

motoneuron at a much higher level than that of the amputation. Peripheral neuron lesions were a common finding in the stump muscles of the below elbow amputees. This was observed *in eight* cases on the extensor side and in six cases on the flexor side of the stump. Thus in one third of these patients the myoelectric signal was pathological in the extensor and the flexor stump

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	Normal EMG	Lower motor neuron lesion	Myopathy or reinnervation	No of muscles available for exam	Normal EMG	Lower motor neuron lesion	Myopathy or reinnervation	No of muscles available for exam
M deltoideus	6	1	—	[illegible]	23	—	—	23
M *biceps* brachii	4	3	—	[illegible]	20	3	—	23
M triceps	2	2	—	4	21	[illegible]	—	23
M brachio *radialis*					18	[illegible]	1	21
M extensor digitorum					13	8	1	
M flexor *digitorum*					15	6	—	21
Total	12	6	—	18	110	21	2	133

the extensor side of the stump and the triceps muscle There were fibrillations in all these muscles and also spontaneous positive potentials of short duration This patient was operated on two years ago Fibrillar action potentials were found in one muscle of another patient who had been operated upon twelve years ago

In addition to the cases in which was found a decided lower motoneuron lesion other deviations in the appearance of the myoelectric signal were observed Thus there was an increased number of polyphasic potentials approximately 10 20 per cent in nine muscles as compared to the about 4 per cent commonly stated in the literature as normal for limb muscles The increased rate of polyphasic potentials was present in the stump muscles of below elbow amputees except in one case A further deviation from the normal EMG was the presence of monotonous motor unit potentials with a duration which was estimated to be slightly increased Such potentials were observed in seven stump muscles of below elbow amputees and in two of above elbow amputees

Figure 8 illustrates a number of potentials of short duration approximately 4 5 milliseconds and an increased rate of extremely polyphasic potentials These potentials were picked up from the same needle position in the brachioradial muscle of a patient who had been amputated for gangrene caused by a septic embolus The EMG findings could be indicative of myopathy but similar changes could be a sign of reinnervation In view of the cause of amputation and of the fact that in this case there was myositis the change in the myoelectric signals was regarded as myopathy

The electromyographic findings in the stump muscle on the extensor side of the forearm and in the brachial biceps muscle varied with the intramuscular

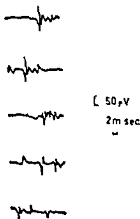


Fig 8 Single motor unit potentials [illegible] the brachioradial muscle in a below-elbow amputee needle electrode in the same position The potentials [illegible] short duration and [illegible] polyphasic potentials

muscles These muscles constitute the muscle pair which so far have been *commonly explored as control sites in electric hand prostheses However the* pattern of a peripheral neuron lesion only appeared in two cases in the brachioradial muscle

Table 12 illustrates the EMG results and their distribution within various muscles of the same patient as related to the length of the stump It can easily be seen that pathological changes of the myoelectric signals were found in both long and short stumps The clinical changes as found in all the patients with short stumps are not in accordance with the pathological EMG changes The table further shows that of all the muscles examined in the amputated extremity only ten below elbow amputees had EMG findings which could be considered as normal In seven other patients a peripheral neuron lesion was found in one muscle only Thus it could be stated that a fourth of the below elbow amputees had pathological myoelectric signals in at least two muscles of the injured extremity

The three muscles which have been examined in above elbow amputees showed a normal EMG in one patient only Three patients had a peripheral neuron lesion in one muscle Half of the above elbow amputees had no normal *myoelectric signals in two of the three muscles* which are the most natural to use as control sites

The changes in the myoelectric signals which are designated peripheral neuron lesions were usually moderate Pronounced lower motoneuron lesion with remaining single large potentials were found in three cases only This is illustrated in Figure 7 where only single very large potential were picked up from the stump muscle on the *flexor side of the forearm in a patient with an* extremely short stump This patient also had a peripheral neuron lesion in

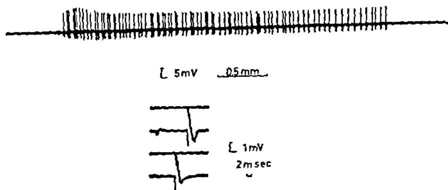


Fig 7 Advanced lower motoneuron lesion The myoelectric signal were picked up by a needle electrode from a small remaining muscle on the flexor side of a short forearm stump The single motor unit potentials was extremely large with an amplitude of about 4 mV

the extensor side of the stump and the triceps muscle. There were fibrillations in all these muscles and also spontaneous positive potentials of short duration. This patient was operated on two years ago. Fibrillar action potentials were found in one muscle of another patient who had been operated upon twelve years ago.

In addition to the cases in which was found a decided lower motoneuron lesion, other deviations in the appearance of the myoelectric signal were observed. Thus, there was an increased number of polyphasic potentials, approximately 10–20 per cent, in nine muscles as compared to the about 4 per cent commonly stated in the literature as normal for limb muscles. The increased rate of polyphasic potentials was present in the stump muscles of below-elbow amputees except in one case. A further deviation from the normal EMG was the presence of monotonous motor unit potentials with a duration which was estimated to be slightly increased. Such potentials were observed in seven stump muscles of below-elbow amputees and in two of above-elbow amputees.

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The electromyographic findings in the stump muscle on the extensor side of the forearm and in the brachial biceps muscle varied with the intramuscular

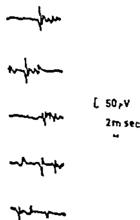


Fig. 8. Single motor unit potentials picked up from the brachioradial muscle in a below-elbow amputee, needle electrode in the same position. The potentials are of short duration and there is an increase of polyphasic potentials.

temperature according to Table 13 The table clearly shows that the intramuscular temperature had dropped in all muscles showing peripheral neuron lesions increased duration or a surplus of polyphasic potential All the myoelectric signals regarded as normal were picked up in muscles with an almost normal temperature In nine cases the intramuscular temperature was 36 C or more Temperatures between 35 and 36 C were noted in fifteen cases Six patients had a very low muscle temperature which may be due to traumatic injuries of the vessels There was no close relation between the length of the stump and the intramuscular temperature Of the six patients who had temperatures below 35 C one patient only had a stump shorter than 10 cm

Table 13 EMG findings in relation to intramuscular temperature of the same muscles

Intramuscular temperatures	EMG findings
36 5	Normal
36 4	Normal
36 4	Normal
36 4	Normal
36 4	Normal
36 3	Normal
36 3	Normal
36 0	Normal
36 0	Normal
35 9	Normal
35 9	Normal
35 8	Lower motoneuron lesion
35 8	Lower motoneuron lesion
35 7	Increased duration
35 6	Normal
35 5	Normal
35 5	Lower motoneuron lesion
35 5	Lower motoneuron lesion
35 4	Lower motoneuron lesion
35 3	Normal (Below elbow Temp in m bic p)
35 2	Normal
35 1	Increased duration
35 0	Lower motoneuron lesion Increased duration
35 0	Surplus of polyphasic potentials
34 7	Lower motoneuron lesion
34 5	Lower motoneuron lesion
34 5	Surplus of polyphasic potentials
34 5	Lower motoneuron lesion
34 3	Myopathy oreinnervation
3[illegible] 0	Lower motoneuron lesion

Statistical analyses of variance reveal with respect to nine right side muscles of the uninjured controls statistically significant differences of the spectrum parameters of individuals as well as of muscles This result holds for all the six spectrum parameters The most important source of variation for all six parameters is to be found within the muscle The next most important source of variation also for all six parameters is the difference between muscles The least important factor—again for all six parameters—is inter individual variation

The fact that interindividual variations are significant implies that individuals having high parameter values for one muscle have high parameter values for other muscles also

Various muscle pairs were compared by means of the *T* method The only pairs displaying no statistically significant spectrum parameter differences at all are m extensor digitorum communis vs mm brachioradialis and deltoideus Nine muscle pairs show significant differences for two parameters only The results indicate a higher low frequency content for the trapezoid muscle and a lower low frequency content of the soleus muscle The mm brachioradialis and deltoideus have the lowest numbers of statistically significant differences displayed by the individual muscles and mm soleus and gastrocnemius have the highest numbers The only muscle pair for which all six spectrum parameter differences are statistically significant is m gastrocnemius vs m trapezius

The detailed investigation of needle position influence which was carried out for the brachial biceps muscle revealed with minor exceptions only no statistically significant differences No significant differences at all were found between the average values of the long head and the average values of the short head

The comparatively small coefficients of correlation between spectrum parameters indicating low frequency content and parameters indicating high frequency content may be a reflection of the existence of different types of motor units

Also on the left hand side muscles of the uninjured controls the statistical analyses of variance showed significant differences between the *mean values* of individuals as well as of muscles This result holds for all spectrum parameters As for the right side muscles intramuscular variation is most important *intermuscular* variation is next most important and interindividual variation is least important The number of statistically *significant* intermuscular differences is larger for the left side than for the right side It is interesting to note that statistically significant parameter differences between the

left and right sides of mm interosseus dorsalis I manus extensor digitorum brevis biceps brachii brachioradialis and extensor digitorum communis take place in the same direction

Temperature measurements revealed no discernible temperature dependence of the spectrum parameters in the long head of the brachial biceps muscle of the 50 uninjured controls Temperature influence can neither explain the power spectrum differences between two needle positions in this muscle nor the difference between the left and right sides

Comparison between muscles yielding normal and neurogenic EMG in amputees was performed for the right and left side respectively of the stump extensor muscles and for the right side of the stump flexor muscle The analyses revealed statistically significant differences for all spectrum parameters except for one of the right side flexor muscle Comparisons between muscles yielding normal EMG in amputees were carried out for mm biceps brachii brachioradialis and the stump extensor muscle of below elbow amputees The analysis showed statistically significant differences between the mean values of muscles for all parameters except for one parameter of the left side When muscles of amputees yielding normal EMG and muscles of uninjured controls were compared statistically significant differences between the parameter values were obtained The significant differences for right side muscles deviated in the same direction as those of left side muscles The low frequency content of the amputee muscles was without exception low Temperature measurements were performed in the stump extensor muscle of 14 below elbow amputees The low frequency content tended to decrease with temperature

Dynamic Spectrum Analysis of Myoelectric Signals in Amputees

The dynamic spectral analysis of myoelectric signals from four different muscles in 27 arm amputees is tabulated in Tables 14 and 15 The percentage of recovered muscles was calculated on the number of cases where a significant effect of the high frequency decay was found The percentage of non affected muscles was calculated on the total number of the muscles examined The values obtained at examination of the amputees was related to the corresponding normal values earlier indicated by *Kadefors Kaiser & Petersen* (1968) except for the muscles on the flexor side of the stump where normal values were lacking (Table 15)

Table 15 shows that there was a difference between the remaining extensor muscles of the forearm stump and the corresponding muscles in normal subjects with respect to the decay of the high frequency components In 53 per cent of the amputees there was no significant decay as compared to 5 per cent

T 11 14 Valu oltam l from a nputees Muscl eff ct and recov ry after 0 30 60 an l 30 se on l respe tively

Effect an l recov ry	Stump mu cle xt n r si le	Stu np muscl flexor si l	M brachio ra l ali	M biceps l racl u
	−4 4 16	3 9 8 4	) " 11	3 I) "
	8 3 14	4 3 _ 1	4 8 −3	−1 1 14
	−1 4 4	1 e e 6	1 1 1 10	) 16 11 8
D_1 D	1 8		10 17 3	4 1 14 1
	) 3		15 8 6	4 _ 5 1
				1 3 e 1)
				_ 1
	−8 0 −3)	−1 − 3 0	0 1 0 3	0 −1 −1 3
	− −3 −1 4	1 −1 0	3 3 − −3	3 − −1 −
	−1 0 −1 4	−1 4 0	0 0 4 0	− " −
D D	4 1 1 0		− 4 −	1) 4 4
	0 0 −		0 0	− −) 0
				−1 0 9
				1
	) 1	1 3 1	−1 −1	0 6 4
	1 4 10	10 − 3 0	4 1 −	3 −3 4 9
	3 3	3 8 4	1 14 1 4	7 10 −3
D D	13 3 3		4 18 −	13 6
	10 1		11 8 3	− 3 4 4
				1 1 19
	10 10 '	8 1 1	−e 8 1 5	1 11 4 8
	0 1 10	1 1 0	− 0 0	3 −1 4 14
	0 4 4	e 3 6 4	7 11 13 6	10 11 −3
D D	14 3 3		4 16 −3	4 13 e e
	(1 1		14) 7	− 1 4
				8 0 4 18
				3
	1 1	1 0 3 1	8 3 10	1 3 1
	0 4 6	10 −1 1 0	3 −1) 1	− 1
	1 3 4	8 3 e	11 11 1 6	10 11 −4
D D	1 4 4		13 −3 1	6 13 16 8
	) 1		14 5 −	1 0 4 6
				) 1 18
				1

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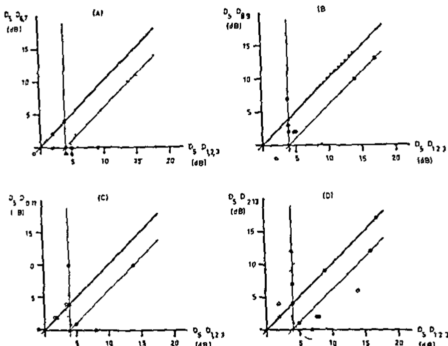


Fig. 9. Recovery of the high frequency decay occurring under the influence of maximum muscle contraction (A) immediately after the sustained contraction (B) after 30 seconds of rest (C) after another 30 seconds of rest (D) after still another 30 seconds of rest. Stump muscle on the extensor side of the forearm, needle electrodes. Open circles represent 18 below elbow amputee. The dotted line encircles normal values with a limit of significance σ

pattern as the three forearm muscles examined on normal subjects by *Kadefors, Kaiser & Petersén* (1968).

The brachioradial muscle was studied on 19 arm amputees, the number of which corresponded to that of the normal series. There was no significant difference at the 5 % level in a *T* test between the amputees and the normal subjects either with respect to the effect or the recovery. The median value of the high frequency decay was 8 dB for the amputees and 11 dB for the normal subjects. The number of non affected cases was 16 per cent for the amputees and 10 per cent for the normal subjects. The effect seems to be lower for the amputees than for the normal series and the difference is almost significant (Fig. 10). The distribution of the normal series with a limit of significance corresponding to 2 σ has been plotted. The figure shows that three values for the amputees lie on or below the 4 dB limit of significant muscle effect. In two of these cases there was advanced atrophy of the brachioradial

Table 15 Effect and recovery with respect to the high frequency band decay. Results from normals by permission from the authors (*Kadefors, Kaiser & Petersen* 1968)

Investigated muscles	D_5–$D_{1,2,3}$ median dB	Immediately recovered per cent	30 s recovered per cent	60 s recovered per cent	90 s recovered per cent	Non affected cases per cent
Stump muscle extensor side	4	0	56	56	56	53
M. extensor digitorum in normals	11	10	32	42	42	5
Stump muscle flexor side	5	17	67	67	67	50
—	—	—	—	—	—	—
M. brachioradialis in amputees	8	6	50	56	75	16
M. brachioradialis in normals	11	6	22	45	61	10
M. biceps med. in amputees	8.5	17	33	50	56	31
M. biceps med. in normals	10	12	55	50	45	5

in the normal series. The significant effect revealed in the extensor muscle by the amputees, however, was quite comparable with that in the normal series (Fig. 9). There was no significant difference either in recovery. In this figure the distribution of the normal series was plotted including values within a limit of significance corresponding to 2 σ. The figure shows that more than half of the values obtained from this muscle in amputees lie closely to the origin of coordinates. Despite the powerful contraction found on clinical examination and the good quality of the signals as observed with the naked eye, these patients obviously could not contract the remaining muscle as much as normal subjects. Furthermore, one case with a muscle effect of -4 dB was excluded from the figure as an adequate contraction was not achieved. In principle the same result was obtained at the examination of the remaining muscles on the flexor side of the forearm stump as on the extensor side. Thus in 50 per cent of the amputees there was no significant reduction of the high frequency components in the myoelectric signals picked up from this muscle. In cases where a significant effect was obtained, the recovery could not be compared with that of a normal series, but in principle followed the same

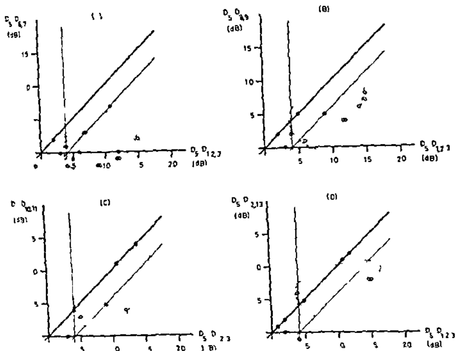


Fig 11 Diagram ... with Figure 9 but showing effect and recovery ... the brachial ... of 6 ... below elbow ... needle electrodes The dotted line ... normal values with the same limit of significance ...

percentage of cases without any significant muscle effect which corresponds to the normal subjects

The results of the four muscles studied in arm amputees by the use of this method are not referred to the EMG findings There was no point in making such a classification of the brachioradial muscle due to the few cases of pathological EMG findings No significant difference was noted in the muscle effect and recovery of the muscles on the flexor and extensor sides of the forearm stump and of the biceps muscle as based on the EMG findings As earlier the conclusions were made after performing a T test with the 5% level of significance

Comparison between Electrodes and Implantation of Micro circuits (Papers II III)

The impedance of the three types of surface electrodes utilized in electrical hand prostheses were measured in different frequency ranges The lowest impedance was found in the Russian electrode which is due to the use of

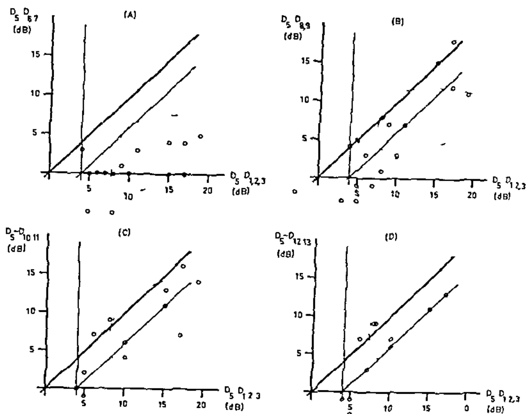


Fig 10 Diagram identical with Figure 9 but showing effect and recovery in the brachio radial muscle of 19 below elbow amputees needle electrodes The dotted line encircle normal values with the same limit of significance 2 σ

muscle and a very reduced strength which involved difficulties for the patients to maintain maximal contraction during 30 seconds

The brachial biceps muscle was studied in 26 amputees five of whom were above elbow amputated As the group of above elbow amputees was very small the observations were not referred to different levels of amputation *Table 15 shows that in comparison with the normal series there was no obvious* difference in the high frequency decay The muscle effect was 8 5 dB in the amputees and 10 dB in the normal subjects *A T* test did not reveal any significant differences at the 5% level in effect and recovery (Fig 11) In 31 per cent of the amputees *there was no significant muscle effect as compared to* 5 per cent in the normal series Among the five examined above elbow amputees *three revealed no significant muscle effect which partly contributed to* the high percentage of non affected cases In two of the five remaining amputees *where there was no high frequency decay of the biceps muscle there was* a pronounced reduction of strength at flexion of the elbow joint In three of the five cases no observations of any importance were made This gives a

membrane sometimes was thin and pale and in others hyperaemic and thickened. The varying degrees of slight hyperaemia which could be found were not related to the period during which the electrodes were implanted. The histological examination revealed a capsule of connective tissue which had developed around the electrodes in varying degrees of thickness. There were layers of histiocytic cells on the surface and some foreign body giant cells and diffuse infiltration by lymphocytes as a sign of inflammatory reaction.

The myoelectric signals received from the implanted electrodes were all except in one case of a good quality. The reason for failure in this case was that a break down in the electronic circuit prevented the electrode from operating after the implantation. According to conventional electromyography the transmitted signals were normal and of a high quality. Repeated analyses proved that the myoelectric signals had been well reproducible during the periods of the experiments. This fact was also found by frequency analysis of the myoelectric signal. Even after several months the shape of the power spectrum was unchanged at different levels of contraction. As compared to needle electrodes a more favourable signal to noise ratio was obtained with the implanted electrodes.

The main problem of protecting the components of the micro circuit from surrounding tissues has been solved satisfactorily by the selected method of encapsulation. No technical failure was due to insufficient encapsulation in this investigation. However there were two cases of small cracks in the plastic material which allowed contact between the semi conductors and the surrounding tissue. The main failure was fatigue fractures in the gold wires at the surface of the plastic layer. These fractures prevented the myoelectric signals from being transmitted in three of the four cases where the electrodes had stopped operating. The fractures of the gold wires were verified radiographically. In one case the myoelectric signals could not be received due to defects in the external system. The external power supply was reliable. However the transmission of energy to the implanted electrode was rather sensitive to the relative positioning of the implanted and the external circuits.

Myoelectric Control of the Electro Mechanical Apparatus (Paper IV)

The results will be given in accordance with the questions discussed in the Chapter of Methods. Table 16 illustrates the off times of nine muscles in a normal series of 30 uninjured males. The importance of learning in this type of test is illustrated by the difference between the off times of two successive tests of the same muscle. The results in Paper IV were thus verified between the two investigations with the exception of a small deviation of the mean in

electrolytic paste The other electrodes the Austrian and the Italian are dry electrodes The Italian electrode has a much higher impedance as compared to the Austrian as a consequence of its smaller area All three types of electrodes have a rather high impedance which at 100 Hz exceed 100 kohm The phase angle within the different frequency ranges has varied least in the Russian electrode

The difference between the half cell potentials of the electrode pairs were measured The maximum value of the polarization difference in a series of ten measurements was given for each type of electrode It was obvious that wet electrodes had considerably higher polarization potential differences than dry electrodes depending on the abundance of dissociated ions which exist with the use of electrolytic paste The polarization potential measured between the signal electrode and its ground plate in the Austrian electrode was considerably higher than the half cell potentials of the signal electrode pair This fact was explained by the signal electrodes and the ground plate being made of different metals which have different contact potentials

The signal to noise ratio in dB of signals from the electrodes under test was measured The centre point distance of different electrodes and the area of the electrodes had a direct effect on the recorded signal to noise ratio Thus this ratio was the most favourable for the Austrian electrodes with the largest centre point distance and the largest picking up area A large centre point distance will give a higher signal potential and furthermore signals from more motor units can be picked up with a large area of the electrode

Spectral analysis of the signals picked up in the signal to noise investigation showed small differences between the spectra of the individual prosthesis electrodes

Using intramuscular electrodes needle electrodes and wire electrodes a higher signal activity within the high frequency ranges was recorded as compared to skin electrodes An implanted electrode had a power spectrum in between the intramuscular and the skin electrodes

Six electrodes were implanted and worn by subjects for varying periods of up to 15 months (Paper III) The volunteers did not experience the short surgical procedures implantation and extirpation of the electrodes as either unpleasant or painful All the patients returned to full work the day after The wounds healed without complications and the amputees could utilize their prosthesis without difficulty for their work and without the pressure from the prosthesis causing any discomfort The final scars were thin and cosmetically quite acceptable

After removal of the electrodes they were all found to be encapsulated by a connective tissue membrane sometimes slightly adherent to the skin but never to the subjacent fascia Macroscopically it was found that the covering

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Myoelectric Control of the Electro Mechanical Apparatus (Paper IV)

The results will be given in accordance with the questions discussed in the Chapter of Methods Table 1b illustrates the off times of nine muscles in a normal series of 30 uninjured males The importance of learning in this type of test is illustrated by the difference between the off times of two successive tests of the same muscle The results in Paper IV were thus verified between the two investigations with the exception of a small deviation of the mean in

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test I This deviation may depend on a modified instruction to the patient before the definite examination By changing the patient s position at the examination (see methods) obvious deviations were caused in the off times of the deltoid muscle on comparison between the two examinations The test conditions were the same and comparable for m extensor carpi radialis longus and for m vastus lateralis The off times of these muscles— obtained at the two examinations—are in good accordance

Table 16 shows that the trapezoid muscle deviated considerably from the other muscles Furthermore it is indicated in the table that there is a tendency towards lower mean values of off time for distal extremity muscles as compared to proximal with the exception of the triceps muscle However it should be emphasized that there was a large dispersion for singular off times The unexpectedly high mean value of the first dorsal interosseous muscle can perhaps be explained by the fact that it proved fatiguing and unnatural to abduct the forefinger continuously during several minutes

The analysis of variance showed significant intermuscular and interindividual effects The significance of the individual effect was weak however In

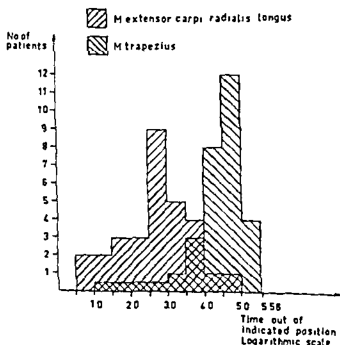


Fig 1 Histogram showing the significant difference in off times in the manoeuverability test between the m extensor carpi radialis longus and the m trapezius of uninjured control The histogram is based on the natural logarithms of the off times

Table 16 Off times for uninjured males in seconds

M extensor carpi radialis I	M extensor carpi radialis II	M flexor dig sublimis	M inter osseous dorsalis	M biceps brachii	M triceps	M del toideus	M trapezius	M vastu lateralis	M tibialis anterior
›2	48	7	8	2›	›2	2	63	18	3
66	18	3	38	10	10		80	›	6
61	"	_0	78	7	21	4	1"6	››	11
6"	13	10	116	24	››	40	7›	(›	›
104	2	4_	(2	90	_3	33	91	2›	91
81	27	8	›	3	3	3	139	68	8
117	_6	16	2	14	9	14	109	12	18
60	14	10	10	71	3	3	7	60	3›
79	4›	7	›9	70	3	21	21	11	23
124	94	20	37	4›	16	79	97	48	11
›	›	110	2	33	23	6	136	69	13
144	33	21	_	17	10	39	130	2	8
46	16	9	36	7	1›	36	106	4›	1
73	8	4	2	3	8	14	"	10	16
80	13	16	43	6	22	2›	99	17	3
127	46	40	29	36	27	1›	›3	86	6
4(	9	3(	6›	28	17	14	109	2›	›
41	4	40	37	_7	11	"6	3›	2	1_
6		3	32	10	16	3"	1››	›	31
31	16	3	26	17›	›3	›0	20	1(	4
8›	2	"	7	›8	1›	3	›"	"4	1›
›8	31	6	›1	7	14	12	"0	34	1(
›4	26	30	43	4›	38	30	(8	68	4
101	69	"	3›	28	4"	12›	1?0	3(	10
(1	4	10	12	(3	10	›9	184	1_	_"
›0	13	3›	8(	8	23	21	(_	70	3
129	18	1›	84	24	18	48	1?›	"	_6
46	40	6	43	20	2	14	94	7›	31
4	19	14	19	_"	"	"0	38	1	_
118	1_	4(	10›	1"	›0	30	8	6	8
Mean									
72 3	2›8	20 2	39 3	33 3	_1 ›	30 9	›3 0	36 ›	14 (
Standard deviation									
34 9	20 7	_1 _	31 2	34 ›	1›4	_8 0	4›_	8 3	›4

Table 1 Off times for amputees in seconds. Mean and standard deviation are referred to below elbow amputees exclusively

Amputation level	Stump muscle extensor side forearm: Normal EMG	Stump muscle extensor side forearm: Lower motor neuron lesion	Stump muscle flexor side forearm: Normal EMG	Stump muscle flexor side forearm: Lower motor neuron lesion	M. biceps brachii: Normal EMG	M. biceps brachii: Lower motor neuron lesion	M. deltoideus: Normal EMG	M. deltoideus: Lower motor neuron lesion
	9		8[illegible]		83		88	
	1				36		119	
		4	1[illegible]		6		–	
	3		[illegible]		13		8[illegible]	
			–		6		3	
				6	10		4	
	8		18		1		3[illegible]	
	11[illegible]		1[illegible]		[illegible]		[illegible]0	
		1	4		30		93	
	1		8		3[illegible]		1	
			30		0		4	
Below		14[illegible]		0		63	63	
elbow			[illegible]		81		4	
	3		0		4		1 1	
				0	4[illegible]		9	
		[illegible]8			6		106	
		43				6		
	[illegible]			16				
				3	11		1	
						4	30	
					11[illegible]		4	
		4		4	4		4	
	4		1		3		3	
						10	[illegible]3	
Above						[illegible]	[illegible]8	
elbow					1		31	
							4	
					11		108	
						8	60	
Mean	[illegible]	41	3 0	18[illegible]	43 3	31 0	[illegible]	–
	35 0		31 3		41		[illegible]16	
Standard deviation	3 4		31 8		30 [illegible]		33	

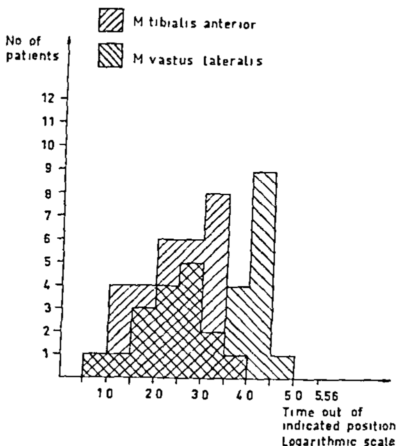


Fig 13 Histogram indicating a certain but statistically non significant difference in off times between a distal and a proximal extremity muscle of uninjured control in the manoeuverability Based on the natural logarithms of the off times

the first place this meant that the means of the natural logarithms of the off times of at least one muscle deviated from one or a few of the other muscles and secondly that there were also deviations between different individuals

The analysis of variance did not show which mean values deviated from each other thus contributing to the significant muscle effect When comparing different types of muscle contrasts it was found that the trapezoid muscle only had a significantly deviating mean value In a histogram (Fig 12) this deviation is clearly demonstrated The mean values of the other muscles were approximately on the same level Thus there were no significant differences in the natural logarithms of the off times between the proximal muscles (mm biceps brachii deltoideus vastus lateralis) and the distal muscles (mm extensor carpi radialis *flexor digitorum sublimis tibialis anterior)* There is a certain difference in the natural logarithms of off times between the anterior tibial muscle and the lateral vastus muscle when illustrated in a histogram (Fig 13)

T'l' 1 Off tim s for ar putees in seconds Mean an l stan lar l d viation are ref rre l to bel w ell ow amput es exclusively

Ar putati n l el	Stu p m usl exten or s l f re rm Norr al EMG	Lower moto n uron l s n	Stu p mu cle fl xor s le forearm Normal EMC	L wer moto n uron l sion	M biceps brachi Normal EMC	Low r mot n uron l on	M d lto leus Normal EMG	Low r moto neuron l ion
	)		8		83		88	
	l				36		119	
		4	16		(			
	3		(		13		8	
					6		3	
				C	10		4	
	8		18		l		3	
	114		1)		)		(0	
		1	4		30		)3	
	l		8		3)		1	
			30		0		-4	
Bkl w		140		0		(3	(3	
ell w			(		81		4	
	3		0		4		1 1	
				0	46		)	
		(8			C		100	
		43				(		
	6			16				
				3	11		1	
						4	30	
					11)		4	
		4		4	4		4	
	4		1		3		3	
						10	3	
						(	08	
Al					1		31	
ll w					5		4	
					11		108	
						8	80	
M	(	44	3 0	18	43 3	31 0	)6	
	3 0		30 3		41			16
St l l l	3 4		318		30(		33 -	

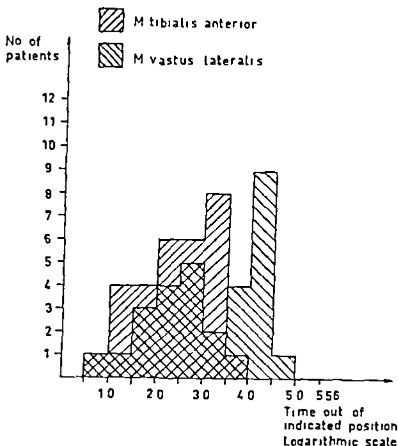


Fig 13 Histogram indicating a certain but statistically non significant difference in off times between a distal and a proximal extremity muscle of uninjured controls in the manoeuverability Based on the natural logarithms of the off times

the first place this meant that the means of the natural logarithms of the off times of at least one muscle deviated from one or a few of the other muscles and secondly that there were also deviations between different individuals

The analysis of variance did not show which mean values deviated from each other thus contributing to the significant muscle effect When comparing different types of muscle contrasts it was found that the trapezoid muscle only had a significantly deviating mean value In a histogram (Fig 12) this deviation is clearly demonstrated The mean values of the other muscles were approximately on the same level Thus there were no significant differences in the natural logarithms of the off times between the proximal muscles (mm biceps brachii deltoideus vastus lateralis) and the distal muscles (mm extensor carpi radialis flexor digitorum sublimis tibialis anterior) There is a certain difference in the natural logarithms of off times between the anterior tibial muscle and the lateral vastus muscle when illustrated in a histogram (Fig 13)

Besides the reservations made above all the off times obtained for the amputees were included in a comparison between uninjured controls and amputees as the EMG findings did not affect the manoeuverability Table 1[illegible] shows that in the group of arm amputees there were higher mean values of off time for each of the four examined muscles as compared to uninjured controls This is clearly depicted in Figure 14 The normal test of the natural logarithms of off times showed however that this difference was significant only for the deltoid muscle

The significant deviation—although slight—between different individuals verifies the clinical impression obtained during the experiments A difference in dexteriority was thus found but no systematical individual factor of importance was found at the statistical analysis

The results of the examination in 30 arm amputated males are seen in Table 17 This table reveals that there were rather few values available for comparison between muscles with a normal EMG finding and those with a peripheral neuron lesion The dispersion of the individual off times is large The statistical analysis showed no significant differences with respect to the EMG findings for remaining extensor and flexor muscles and the brachial biceps muscle in below elbow amputees In above elbow amputees the brachial biceps muscles could not be investigated statistically with respect to the EMG findings due to the small number of observations Thus the off times obtained for the above elbow amputees from the brachial biceps muscle are excluded from the statistical analysis in a comparison between controls and amputees

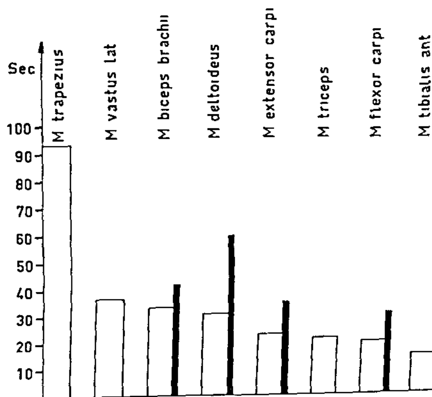


Fig 14 Diagram showing the off times in seconds obtained from different muscles in uninjured (open columns) and arm amputees (filled thin columns) For further discussion see the text

used Practical application of the electric hand prosthesis showed that the mechanical irritation existing with surface electrodes may cause sores if the sensibility of the stump is deficient When the sensibility is normal and the subcutaneous tissue of the stump is satisfactory dry skin electrodes will be tolerated even during long standing daily use In many below elbow amputees the remaining pronation and supination cannot be utilized due to technical fitting problems of the prosthesis In order to offer the patient a functionally improved prosthesis it would be desirable to achieve a normal positioning of the hand That type of prosthesis should be possible to control with a minimum of effort and unconsciously after some time of practice Perhaps an active pronation can be obtained with signals picked up from implanted electrodes in the m pronator teres Picking up separate activity from deep lying muscles a possibility offered by implantable electrodes is perhaps more realistic than creating control sites by other surgical procedures

The impaired mobility of elbow and shoulder joints in a number of amputees is not of a magnitude which does prevent the use of a prosthesis The physical strength is only in singular cases reduced to such an extent that it would be of any practical importance especially as the prosthetic hand always will be the assisting hand in relation to the normal hand

The myoelectric signals picked up from different muscles in an amputated arm are often pathological according to conventional electromyography The changes—a peripheral neuron lesion in a large number of muscles—which were recorded in this series are in accordance with those found by *Petersen* (1966) in 50 arm amputees The reason of this is probably due to the peripheral neuron being injured in connection with the trauma or at the operation The extent of the pathological changes depends on the level at which the nerve has been damaged Fibrillar action potentials rarely occurred which is due to the fact that most of the lesions antedated the examination by several years In fresh amputated stumps denervation potentials probably appear much more often in muscles showing peripheral neuron lesions In the remaining muscles of very short stumps large single potentials have been found in a few cases This is probably a sign of a so called sprouting phenomenon which means that growing terminal nerve fibres belonging to a certain motor unit will contact muscle fibres belonging to another motor unit The number of muscle fibres in a motor unit of that kind will become larger at the same time as the spatial dispersion increases In practical application of simple electric hand prostheses with on off control the interesting result was obtained that these large potentials were satisfactory as control signals This is the more remarkable since only single potentials could be detected even when surface electrodes were used

An increased motor unit dispersion due to sprouting results in more poly

CONCLUDING REMARKS

During the latter decade myoelectric signals have been utilized in practice for control of electric hand prostheses and have furthermore served as control signals in stimulating paretic muscles. The investigations performed earlier involving a study of the myoelectric signal, plotting of the control sites available and assessment of the ability to control man-machine systems were based on normal subjects. However, the myoelectric signals picked up from the patients who will utilize them in the future must be studied and accurately characterized. In this work the characteristics of the myoelectric signals in arm amputated males and normal individuals were investigated. The relative characteristics of different types of electrodes were examined. The description of the myoelectric signal thus obtained permits the signal to be optimized by suitable filtering before electronic application in prosthesis control.

It is the high unilateral and bilateral arm amputees who are in great need of multiple control sites to control prostheses with several degrees of freedom. Clinical findings revealed, however, that the stump muscles of above-elbow amputees are atrophic and retracted and that the triceps muscle was absent in several cases. The shoulder muscles can also be considerably reduced. Asymmetrical shoulders and scoliosis of the thoracic spine are practically always present in above-elbow amputees, which was also pointed out by *Solonen* (1965). The result of these findings is, unfortunately, that only a limited number of control sites are available in above-elbow amputees. It is possible that by attaching the stump muscles distally in order to prevent retraction and atrophy (*Weiss* 1960, 1966) the functional end result will be improved. If the stump is not too short in below-elbow amputees the muscles which are not retracted will only be slightly reduced. Anyhow, it was found that these remaining muscles can be gradually retracted when they are continuously used to control an electric hand prosthesis. A myoplastic amputation procedure where the muscles are attached distally may also for this reason be more attractive. This procedure is believed to give a better stump with less pain, normalized circulation and temperature, less decalcification and a better skin (*Dederich* 1963).

The impaired sensibility which was noted in this series—especially in the above-elbow amputees—must be considered if surface electrodes are to be

Kadefors Kaiser & Petersen (1967 1968) modifications of the power spectrum due to sustained maximum muscle contractions were studied on amputees The present investigation shows these modifications to be of such a magnitude that they should be taken into account in the design of myoelectrically controlled prostheses

The other method *Kaiser & Petersén* (1963 1965) has been used in an extensive study (Paper I) of power spectra for moderate muscle contractions of short duration This investigation demonstrated the existence of statistically significant intramuscular intermuscular and interindividual power spectrum differences The most important source of the differences consistently was intramuscular variation This discovery further underlines the necessity of preprocessing the myoelectric signal in suitable filters It also implies that individual alignment of these filters may be necessary in order to achieve optimum control

At an investigation of three commercially available skin electrodes in myoelectric hand prostheses characteristics such as impedance polarization instability signal to noise ratio and spectral properties were studied In general it can be said that skin electrodes used in the control of myoelectric prostheses should have a low impedance low polarization instability high signal to noise ratio and that the reproduction of the signal activity within high frequency ranges should be great Furthermore the chemical and mechanical irritation of the skin should be insignificant It is obvious that the electrodes which were available at this investigation did not fulfil these demands

The results of micro circuit implantation show that the minor surgery required was easy to perform and caused no subjective discomfort Implantation in the human being of the plastic material selected can thus be tolerated for at least one year Due to the tissue reactions it would be justified to carry out further research work in producing more suitable material Silicone rubber (Paper III) or ceramics (*Kelly* 1968) have been discussed From the technical point of view no failure was due to insufficient protection of the components either mechanically or chemically However there were small cracks in the plastic material in some cases which may have increased the tissue reaction The myoelectric signals transmitted via the implanted electrodes were of a high quality and reproducible during long periods Consequently it is obvious that the signals are not affected by the electrode being encapsuled in a connective tissue membrane

The important failure found in this investigation was due to fatigue breakdown of the gold wires which maintained contact with the tissue This problem can perhaps be overcome by using thin flexible wires instead As a result of our experience a modified electrode of that type has been designed The

phasic potentials Inactivation of motor units and synchrony of remaining units may according to *Pinelli & Buchthal* (1953 *b*) also contribute to the abundance of polyphasic potentials in lower motoneuron lesions The low *intramuscular temperature of the stump* may also contribute to the increased number of polyphasic potentials by non synchronization of otherwise simultaneously activated muscle fibres within the same unit (*Buchthal Pinelli & Rosenfalck* 1954)

In one single patient an EMG pattern of myopathy displaying a large number of short duration potentials and an excess of polyphasic potentials was observed This patient probably had myositis in the stump muscles due to the serious arm infection which caused the amputation

In the stump muscles potentials have also been observed with a certain—subjectively assessed—increased duration These potentials were found when the intramuscular temperature was low Several authors have shown earlier that a reduced intramuscular temperature causes an increase in the duration of the motor unit potential This was believed to result from a decreased conduction velocity along the terminal branches of the nerve fibres and the muscle fibres (*Pinelli & Buchthal* 1953 *b*) The low intramuscular temperatures which are found in amputation stumps probably depend on a change in the circulation and comparatively reduced muscle bundles *Eriksson* (1965) showed by means of angiography that the blood supply to leg amputation stumps may be irregular and that the muscle volume is reduced The same author mentioned that the amputation stump painful to the patient had a greater mean blood supply at rest as compared to the cases without pain Furthermore he pointed out that the abundance of serpentine vessels did not necessarily mean that the tissues are well nutritioned but that these vessels may act as shunts This is also in accordance with the investigations of oxygen tension pO present in the venous blood of amputation stumps (*Hulth & Hogstrom* 1961)

An essential point in myoelectric control of externally powered prostheses and orthoses is the dynamic range of the control *i e* the number of well defined separate levels of the output Large dynamic output range requires that the full contraction range of the control muscle be utilized Investigations on the properties of the myoelectric signal can thus not be limited to the individual motor unit potentials since these are discernible at the very weak contractions only Even a slight increase of muscle contraction causes the myoelectric signal to take on the character of random noise Thus the control properties of the myoelectric signal can be characterized throughout the dynamic range by means of its power spectrum

Two definite methods have been used for measuring power spectra of myoelectric signals from a great number of muscles With the aid of one method

Th re is no doubt a changed sensory information when part of an extremity is mi in, with an impaired ability to move the extremity with proximal muscles This should be borne in mind as simulating tests with man machine systems are generally performed on normal subjects in prosthetic research The results of these tests are not relevant for amputees with re pect to certain mu cles An analysis necessary to obtain a myoelectrically controlled pros the is with several degrees of freedom concerns the ability of a patient to utilize a number of control sites independently of each other The activity present under normal daily and professional conditions in the muscles pos ible as control sites must be investigated These complex functions must be subject to research before the possibility of controlling a prosthesis with si nals from single motor units can be established

favourable signal to noise ratio depends on the low noise contribution obtained by this method Consequently the implanted electrodes are superior to the conventional ones especially at low contraction levels A limited band width of the receiver has caused a reduced signal activity within high frequency ranges An improvement can be achieved without difficulty by increasing the band width of the receiver Both from the technical and the biological points of view, the existing miniaturization was adequate Security of the function is however necessary during a considerably longer time which should be the aim

When considering the function of the electro mechanical apparatus for the manoeuverability test it can be assumed that the position of the fly wheel is characterized by an approximately normal distribution The assumption that the position of the wheel is normally distributed gives a mathematically univocal relation between the off time recorded and the standard deviation The instabilities of the input signals of the apparatus can be described by their standard deviations (standard deviation of programme signals=0) The relation between the input and output standard deviations are functions of frequency inasmuch as rapid variations are damped and slow variations are stressed by the apparatus This can also be described as a time delay of the apparatus It is a general control system experience that time delays tend to create oscillations The ability to manoeuver the apparatus can partly be regarded as the ability to predict the next phase which is a cerebral function The apparatus obviously does not separate the cerebral component and the muscle effect but measures a combination of these two factors As a designation of this complex function the term manoeuverability was introduced The above reasoning reveals a relation between manoeuverability and recorded off time

The analysis of the ability to manoeuver an electro mechanical apparatus by myoelectric signals shows that the trapezoid muscle differs from a number of extremity muscles In that connection it should be noted that this muscle participates in the gross activities of the statics of the body The endurance of the muscle is greater than its ability to perform rapid and precise movements The difference in the number of muscle fibers per motor unit and in the existence of functionally different types of muscle fibers may explain this result of the trapezoid muscle The moderate pathological changes present in the muscles of several amputees do not affect the manoeuverability These remaining stump muscles are thus cerebrally well controlled despite many years having elapsed since the normal function of the muscle ceased

Arm amputees have greater difficulties to manoeuver a man machine system with certain mu cles as compared to normals This can partly be explained by less daily activity and less training of the muscles on the amputated side

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ERLAND LYSELL

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An Experimental Study on Autopsy Specimens

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F m h Dep tm t f Orthop di S gery U ersity f Gö b g S den
(H d Profes C l Hirsch)

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An Experimental Study on Autopsy Specimens

By

ERLAND LYSELL

MUNKSGAARD
Copenhagen 1969

From the Swedish

by

Lois Goldie Carlson

GÖTEBORG 1969
ELANDERS BOKTRYCKERI AKTIEBOLAG

CONTENTS

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Gothenburg in March 1969
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INTRODUCTION

Many people are occasionally or repeatedly subjected to pain and impaired motion in the neck often combined with radiating pain in the back of their head shoulders arms or chest In a Swedish population the percentage was stated to be 70 (*Hult* 1954)

These symptoms have been ascribed to various types of congenital degenerative or post traumatic changes of the cervical spine During latter decades numerous investigations have been published on the pathomorphology diagnostics and therapy

The diagnosis to the greater part was often based on studies of the function of the cervical spine It has been maintained that changes in the function either would be the cause of the disturbances or signs of processes which could result in pain However on perusal of the literature the information found about the normal function and its relation to degenerative changes is sparse This particularly applies to the pattern of motion

The purpose of this investigation was mainly to illustrate the normal pattern of motion and its variations due to degenerative changes by studying the possibilities of motion in an autopsy specimen series This study included all the interspaces between the second cervical vertebra and the first thoracic vertebra

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REVIEW OF LITERATURE

A Earlier Methods for Measuring Intersegmental Motion in the Spine

1 *Motion Studies on Autopsy Specimens*

Ever since Galenus and Vesalius time the motion of the spine has been studied This survey is limited to the in principle different methods reported and employed for intersegmental measurements of motion For a comprehensive review of the literature the reader is referred to *Fluard* (1939) and *Andersson & Ekstrom* (1940)

The first real measurements were performed by *Weber* (1827) In three spinal specimens he dissected the spinal and transverse processes and inserted metal pins and then studied the motion of the pins while bending and stretching the specimens manually The method of measuring angles or distances between pins inserted in the vertebrae has since then been employed repeatedly inter alia by *Volkman* (1872) *Meyer* (1873) *Hughes* (1892) *Lovett* (1905) *Keene* (1906–07) and *Lucas & Bresler* (1961) *Ball & Meyers* (1964) used the method to study the cervical spine They radiographed the specimen at maximal flexion and extension and measured the angle between the pins on the radiographs

Virchow (1928) studied the motion of the cervical spine in the sagittal plane in two specimens by making plaster impressions of the specimen in a neutral position and in manually caused flexion and extension The specimens were macerated and split in the sagittal plane and placed in the different plaster impressions and the range of motion could be measured *Vorogodsky* (1911) on four specimens demonstrated the intersegmental range of motion by testing the entire spine step by step as follows A vertebra was fitted to a measuring apparatus and the super jacent vertebra was secured in a movable ring equipped with dials which indicated the motion at load in different directions

The same method in principle was used by *Andersson & Ekstrom* (1940) for measuring motion in three thoracic and lumbar spine specimens The recording was performed by means of a light ray which in small mirrors on the movable ring was reflected to a scale Simul

TERMS AND DEFINITIONS

The terms and definitions mentioned below have been used throughout

The cervical vertebrae are numbered in the conventional way C2–C7

The first thoracic vertebra is designated Th1

An interspace is identified by the numbers of the two surrounding vertebrae, for instance C4/5

The motion of a segment is identified by the number of the vertebra above and the motion of this vertebra is always related to the subjacent one

Extension is equal to the motion in the sagittal plane dorsally directed

Flexion is equal to the motion in the sagittal plane, ventrally directed

Latero flexion is equal to the motion in the frontal plane to the right or the left

Rotation is equal to the motion in the horizontal plane to the right (clockwise) or to the left (anti clockwise)

The measuring points are designated A=anterior P=posterior R=right and L=left

For statistical analyses the Student s T test was used when no other indication is given

through the upper and lower contours of the vertebral bodies If the endplates of the vertebral bodies appeared as ellipses he used their major axes as a measuring line The maximum error was stated to be 2

Buetti Bauml (1954) used carbon paper to copy the contours of two vertebrae from the flexion radiograph to the extension radiograph and was careful to superimpose the two lower contours The position of the upper two vertebrae corresponded to the motion Lines were drawn through the posterior contour of the vertebral bodies and the angle between these lines indicated the range of motion

For clinical use *Penning* (1968) placed a smaller film of the extension radiograph on top of the larger flexion radiograph The contours of the two C7 views were made to coincide and he drew a line along the edge of the top film This procedure was repeated for each vertebra The angles formed between the lines represented the intersegmental range of motion

Albers (1954) expressed the total motion of the cervical spine in the angle formed between two lines drawn through the posterior contour of C7 and C2 The intersegmental motion was illustrated by indicating the angle between the vertical axis of C7 and a line drawn from the point of intersection of this axis and the upper endplate of C7 to the centre point of the lower endplate of each vertebra *Schalimt ek* (1958) who measured the motion of the lumbar spine in the sagittal and frontal planes drew lines through the distal contour of the bodies *Kottke &* *Mundale* (1959) used the same method in principle for the cervical spine while *Colachis & Strohm* (1965) measured the distance between the anterior and posterior corners respectively of the adjacent vertebral bodies This is a mode of recording extension and compression of the anterior and posterior parts of a disc in connection with motion By means of cine radiography the ranges of motion in the atlanto occipital and the atlanto epistrophic articulations were measured (*Fielding* 1957) Accurate measurements were difficult to carry out however due to the ever changing view and the enlargement (*Fielding* 1964 *Hirsch et al* 1964 *Penning* 1968)

B Pattern of Motion in Cervical Spine

The pattern of motion in the cervical spine depends on the structure and shape of the discs and the intervertebral joints and the combination of the changed positions which may appear The system is also

taneously, the magnitude and direction of the loading force were recorded

Werne (1957) analysed the pattern of motion in the occipito atlanto axoid joints by reading the movement direct on protractors, fitted to the specimen

The most accurate measurements of intersegmental motion were carried out by *Rolander* (1966) For his experimental study of the pattern of motion in the lumbar spine and the stabilizing effect of fusions he used extensometers, the movements of which were recorded by differential transformers

2 Motion Studies on Living Subjects

Direct measuring on living subjects by employing different types of goniometers, generally fitted to the head cannot and are not intended to reveal the motion of the individual segments This applies even if, for instance *Stookey* (1966–67) believed himself capable of determining intersegmental impairment of motion merely by means of manual examination Attempts have been made to record the motion of the individual vertebrae by fitting various types of indicators to the skin over the tips of the spinal processes (*Lohr* 1890, *Lovett* 1905) For several reasons this method must be extremely inaccurate and according to *Lohr* (1890) was not suitable for the cervical spine due to the comparatively great distance between the spinal processes and the skin

Radiography has so far, proved to give the best results when studying the motion of the spine in vivo *Virchow* (1928) was one of the first to use this procedure As a supplement to his earlier described investigation on specimens he examined one person by means of radiography Two radiographs were taken of the cervical spine one in flexion and one in extension From the radiographs he copied the vertebral bodies and the pedicles on a paper After selecting suitable measuring points he connected them by drawing lines When the two copies were placed on top of each other the deviating angles of the lines as seen on the copies could be measured *Dittmar* (1930) used the same method for the entire spine He completed the examination with a radiograph in neutral position and studied the latero flexion in the same way

In principle the same method was then used by many authors and has been called functional radiographic examination or 'Functionelle Rontgenuntersuchung (*Penning* 1968 *Schmorl & Junghanns* 1951) The method of estimating the motion varies *Bakke* (1931) drew lines

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B Pattern of Motion in Cervical Spine

The pattern of motion in the cervical spine depends on the structure and shape of the discs and the intervertebral joints and the combinations of the changed positions which may appear The system is also

affected by the ligaments and the joint capsules Thus, *Ball & Meyers* (1964) found close correlation between the range of motion and the extensibility of the posterior soft collagen structures

In relation to its surface the cervical disc is comparatively high which according to *Fick* (1911) partly explains the large range of motion as compared to other parts of the spine The two vertebral endplates are cranially convex in the sagittal plane, and caudally convex in the frontal plane and together with the disc form a saddle syndesmosis (*Fick*, 1911)

The surfaces of the intervertebral joints are almost perpendicular to the sagittal plane (*Fielding* 1964 *Penning*, 1968) and the mean inclination to the frontal plane is 45° The cranial facets are directed backwards upwards and the caudal forwards downwards The joint capsules are easy to extend and permit great mobility

The following description of the pattern of motion is based on published reports of a few anatomical specimens (*Winslow*, 1730 *Weber* 1827, *Fick* 1911) and radiographs of subjects With the exception of cineradiographic examinations (*Fielding* 1957 and 1964, *Jones* 1960) the reports are based on exposures in extreme positions and in a neutral position (*Dittmar*, 1931, *Bakke*, 1931 *Hadley* 1944 and 1956 *Exner* 1954, *Buetti Bauml* 1954 *Colachis et Strohm* 1965 *Penning* 1968)

In flexion a cervical vertebra tilts and slides forward over the subjacent one There will then be a ventral compression and a dorsal expansion of the disc The spinal processes are separated from each other and spread like a fan Simultaneously the caudal intervertebral joint surface of the vertebra slides upwards forwards over the cranial joint surface of the subjacent vertebra The joint space widens into the shape of a wedge with the base in a dorsal direction

Most authors found that the tilting and sliding occurred at the same time However *Jones* (1960) reported that flexion began with the tilting and the sliding followed later In extreme flexion the joint facets were almost subluxated (*Fielding*, 1957) while *Penning* (1968) mentioned that they covered each other at least 5 mm

When the cervical spine was extended the pattern of motion was reversed On the other hand *Dittmar* (1931) stated that the C6 pattern was inverted inasmuch as at flexion it slid backwards and at extension forwards over C7

The sliding combined with tilting caused the anterior and the posterior borders of the vertebral bodies in extreme positions to form an uneven curve and instead appear in a stepped shape This sliding was

normal in the cervical spine but was believed to be a sign of disc degeneration in the lumbar spine (*Knutsson*, 1944)

The centre of motion is according to most authors placed in the body of the subjacent vertebra as opposed to other portions of the spine in which it is believed to lie in the disc (*Fick* 1911) According to *Fick* (1911) and *Strasser* (1913) the axis is in the centre of the vertebral body *Penning* (1968) mentioned that the axis of C2 is found in the postero caudal portion of the body of C3 but in the lower portions of the cervical spine its position gradually becomes more anterio cranial The axis of C6 lies in the centre of the upper C7 endplate When *Dittmar* (1931) tried to construct the axis of motion he assumed it to lie within the disc Thus he obtained different axes for different parts of motion *Exner* (1954) and *Hjortsjo* (1959) maintained that the axis is placed in the nucleus but according to *Exner* the nucleus moves towards the convex side during motion thus the axis of motion also moves This seems to fit *Lolander's* (1966) findings of a very large number of motion centres in the lumbar spine

The movements in the frontal and horizontal planes are dependent on each other as latero flexion always is combined with rotation in the same direction and vice versa (*Lovett* 1905 *Vongorodsky* 1911 *Dittmar* 1931 *Exner* 1954 *Buetti Bäuml* 1954 *Fielding* 1964 *Hin & Erdmann* 1967 *Penning* 1968)

When a vertebra is latero flexed the disc on the concave side is compressed and expanded on the convex side and simultaneously distorted On the concave side the caudal intervertebral joint surface slides backwards downwards and is pressed against the subjacent joint surface On the convex side the joint surface slides upwards forwards and the joint space widens *Bakke* (1931) mentioned that the vertebral body in latero flexion slides on the disc slightly towards the convex side

Even if the range of motion is reported merely as latero flexion or rotation the combined motion is optimal (*Hjortsjo* 1959) *Fick* (1911) studied the planes of the intervertebral joints and found that an assumed line in the sagittal plane between the joint surfaces perpendicular to them would pass through the centre of the subjacent vertebral body He believed this line to be the axis of combined motion the total range of motion around the axis amounting to 180 *Vongorodsky* (1911) found that in two specimens the range was 76° and 154 respectively

The lateral portion of the cervical spine the so called unco-vertebral region with the uncinate process thrusting upwards from the lateral

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The lateral portion of the cervical spine the so called unco vertebral region with the uncinate process thrusting upwards from the lateral

portion of the upper endplate differs in shape from other portions of the spine

It has been maintained that this region is a true synovial joint (*Trolard*, 1893, *Compere et al* 1958–59 *Jackson*, 1965) Most investigators however, are aware of the fact that changes simulating a joint, merely are very early fissures formed laterally in the annulus (*Töndury* 1943 1959, *Hall*, 1965, *Ecklin*, 1960 *Hirsch et al* 1967) These fissures may be an adaptation caused by motion in that area (*Töndury* 1943) The degenerative changes appear first in the cervical discs in this region (*Hirsch et al* 1967)

The uncinate process may be of importance for the pattern of motion in the cervical spine It has been mentioned that the process prevents lateral or backward subluxation and serves as an obstacle of latero flexion At the same time it acts as a guide rail for extension flexion (*Frykholm* 1951, *Compere et al* 1958–59, *Ecklin*, 1960, *Penning*, 1968)

C Range of Motion in Cervical Spine

The cervical spine is the most mobile portion of the spine The mean range of motion is according to *Hjortsjo (1959)* extension 55° (if the motion between the occiput—C1–C2 is included 70°) flexion 65° (80°) latero flexion 15° (20°) at each side and rotation 45° (70°) in either direction The individual variations are very large

Measurements of motion were generally based on a neutral position In specimens the neutral position was called Eigenform (*Fick* 1911) and was defined as the position of the cervical spine when it is unloaded and deprived of all musculature The existing lordosis is believed to depend on the wedge shape of the discs with an anterior base and on the vertebral bodies being higher ventrally than dorsally

The neutral position of living individuals is difficult to define Many authors claimed that in the neutral position the vertebral bodies are situated in a symmetrical lordotic curve (e g *Hadley* 1949) *Albers* (1954) and *Zeitler & Markuske* (1962) found different types of neutral positions in different individuals There is also a straight shape of no pathological significance *Fineman et al*, (1963) showed that the normal lordotic pattern may be changed into a linear or kyphotic shape merely by lowering the subject s chin slightly at the examination A comparison between different authors requires an accurately defined neutral position However this is not the case *Albers* (1954) and *Dittmar* (1931) stated a comfortable position *Penning* (1968) pointed out that the lower

margin of the orbita should lie in the same horizontal plane as the external auditory meatus. *De Seze et al.* (1951) preferred that the occlusion plane of the teeth should be horizontal, while other authors do not define the neutral position. This variation may explain differences and statistical contradictions when the range of motion is classified in extension and flexion (Table 1). *Bakke* (1931) measured the extension to be four times the flexion, while *Kottke et al.* (1959) reported the flexion as slightly larger than the extension.

The occipito-atlanto-axoid joints were obviously included in the clinical examination of patients. Using goniometers of different types (*Bennet et al.* 1963, *Buck et al.* 1959) or other technical devices (*Volkmann* 1872, *Ferlic* 1962, *Schoening et Hannan* 1964) mean values were obtained, on the whole, in accordance with those of *Hjortsjo* (1959).

In order to demonstrate the intersegmental range of motion, the most common method is to measure on radiographs. Views of extreme extension and flexion and sometimes also a neutral position view have been compared. Most authors expressed the total motion in the change of angle between the sagittal diameters of the top and the bottom vertebrae. Others used the angle which is described by a line between the anterior corner of Th1 and C2 (*Colachis & Strohm* 1965) or the distance between the tips of the spinal processes (*Otto* 1955, *Rossler & Schmeisser* 1957–58). The results of the various methods are difficult to compare.

An assessment of the entire cervical spine motion is for several reasons not sufficiently informative (*Kottke & Mundale* 1959). Segmental immobilization due to post-traumatic or degenerative changes, for instance, may often increase the mobility of adjacent segments (*Fielding* 1964). The intersegmental ranges of motion as reported in the literature are tabulated (Table 1). The few investigations carried out to the greater part deal with positions in the sagittal plane.

The examinations of specimens are few and mainly of an early date. The range of motion in the sagittal plane was measured on 18 specimens, in the frontal plane on 5, and in the horizontal plane on 6 specimens.

It is difficult to compare the results as the methods differ and as no details are given about the specimens. *Ball & Meyer* (1964) who were responsible for half of the published series dealing with measurements in the sagittal plane, radiographed the specimens in one plane. They have not eliminated the sources of error which could be involved with this procedure.

The intersegmental motion on living subjects was measured on radio-

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	(			C6			C7			S in C C8		
	I t	Fl	T tal	F t	Il x	Total	Ext	Flex	T tal	Ext	Flex	Total
1	ry l g 6 5	⟩ 5 13	1 16 9 17 (14) 0	1	ll 7 5 1	8 5 1 8 14 (14 4) 17 0	ry sm ll 4	5	8 1 (6 –17) 10 4			0 75 80
3						—			—	60 0	16 0	— 100 0 80 5
4						4 0			— 10	64	16 3	8 0
5				6 5	10 5	13 5 17 0	6	4 0	—			5 5–104 5 91
6	16	10 5		0 4	13 4	3 6 (13) 18			—	58	33 0	
7	10 6	3 8	(18 8)	5		1 0 5 17			—	30	48	84 1 3 0
8			4 5– 3 5	7 5	11	6			—			101
9						18			—			87 5
10	18 5			1	5	13 (17–) 3			—			
11	11	10	(0 34)	7 5		(13– 9) 1 5			(4 1) 8			
1			(10– 9)	3		(6–) 1						
			(10–)	1								
13												

	R gl t	Left	Tot l	R gl t	I ft	Tot l	Right	I eft	Total	R gl t	I ft	Total
			8 44	5 07	3 58	0 17	9 0	4 5	5 0–17	10 70	7 6	7 54 6
14		4	0 16							13		
15								8		–1 8		
16	1 0			0								
17	5 0			4 0								

	Total	Total	Total	Total
	33 8	15 3	13 0	130 7
18	0–13	0 14	0 13	
19				

Author		No	Age	C2				C3				C4			
EXTENSION FLEXION				Ext	Flex	Total		Ext	Flex	Total		Ext	Flex	Total	
Measurement on specimens															
1 Weber	1827	3	?	almost none				very big				very big			
2 Virchow	1928	2	?	4–6	3–7	7–13		3	5 5–9	8 5–12		7–9	7 75–8	15–16 75	
3 Novgorodsky	1911	4	53–62			12–18				11–21				8–14	
4 Ball & Meyers	1964	5	21–70			(4 5–12 5)	9 5			(7–20)	15 1			(12 5–28)	18 1
Measurement on radiographs of living subjects															
5 Virchow	1998	1	?				16				20				20
6 Dittmar	1931	?	?	1 5	9		10 5	17	16		23	15	7		22
7 Bakke	1931	15	13–61	9 6	3 0		12 6	12 3	3 1		15 4	12 3	2 8		15 1
8 Buetti Bäuml	1954	30	10–40			(5–18)	10 5			(13–23)	17			(16–28)	21
9 Exner	1954	4	18–58			2 5–13				9 5–22 5				8 0–28 5	
10 De Sèze & al	1951	9	15–55	8	5		13	10	5 5		15 5	12	7		19
11 Kotke & al	1959	78	young men	3	8		11	9	7		16	8	10		18
12 Zeitler &		24	11–14			(18–23)	17 5			(15–38)	25 5			(22–39)	29 5
Markuske	1962	24	15–18			(4–22)	13 5			(13–29)	21			(10–31)	22 5
13 Penning	1968	?	?			(5–16)	12 5			(13–26)	18			(15–29)	20
LATEROFLEXION				Right	Left	Total		Right	Left	Total		Right	Left	Total	
Measurement on specimens															
14 Meyer	1853	1	23	5 22	6 38		14	4 20	6 47		11 07	5 12	6 48		12
15 Novgorodsky	1911	4	35–62			11–20				9–15				0–16	
Measurement on radiographs of living subjects															
16 Dittmar	1931	1	?	4 5				3 5				3 5			
17 Bakke	1931	5	13–23	3 5				4 8				4 5			
ROTATION						Total				Total				Total	
Measurement on specimens															
18 Hughes	1852	–	20–?				28 2				27 7				2 7
19 Novgorodsky	1911	4	35–62			12–22				8–14				[illegible]	

	C5			C6			C7			Sum C5–C8		
	Ext	Flex	Total	Ext	Flex	Total	Ext	Flex	Total	Ext	Flex	Total
1	ry l g			small 1	7 1 5	8 5–17 5	very small 4	5 5	8 1	1 5		80 5
	+ 0 5	9 5 13 5	15 10			8–14			(6 17) 10 4			
			9 17			(14 4) 1 6						
3			(14 5) 0									
4						—			—			—
			—						—	60 0	46 0	100 0
5			6	10	13 5	4 0			10	64	16 3	80 5
6	16	10 5	0 4	13 4	3 0	17 0	6	4 0	—			89 0
7	16 0	3 8	5			(13) 18			—			-104
8			(18 8)			1 0 5			—	8	33 0	31 5
9			4 5- 3 5			17 5						
10	18 5	9	7 5	11	6				—	36	48	84
			1		13	18			—			1 3 0
11	11	10	(0 34) 7 5			(17) 3			—			101 5
l			(10) 3			(13 9) 1 5						87 5
13			(16 0) 1 5			(6) 15			(4 1) 8			

	Right	Left	Total	Right	Left	Total	Right	Left	Total	Right	Left	Total
						9 05	4 5	5	10 0	-7 0	7	4 6
14		4	8 44	07	3 8	0 17			0–17			
15			0 16							13		
				0			8			1 8		
16	1 0			4 0								
17	5 0											

	Total	Total	Total	Total
			13 0	130 7
18	33 8	1 3	0–13	
19	0–13	0 14		

graphs The table shows that the largest range of motion in the sagittal plane almost regularly was found between C5–C6 This was verified by other authors omitting statistical data (*Hadley*, 1949 *Fielding* 1957, *Colachis & Strohm*, 1965) There is a considerable individual dispersion within the various segments often more than 10° within one segment The reason may be that the intersegmental range of motion depends on the mode in which the movement is performed *Jones* (1960) showed that the range varied if the flexion was begun or ended by drawing in the chin Despite projection and method errors the values indicated for the intersegmental total range of motion however seem to be in comparatively good accordance

Intersegmental measurements of motion on radiographs are extremely inaccurate with respect to other directions except for the sagittal plane This is illustrated by the fact that with two exceptions no numerical data are given *Dittmar's* (1931) values were published merely as notes on a sketch *Penning* (1968) stated that the total latero flexion in one direction was 30°, but that it was unevenly distributed over the segments He indicated the rotation at 8–10° per segment

D Degenerative Changes and Motion

Degenerative changes of the cervical spine begin very early and are primarily localized to the annulus fibrosus in the unco vertebral region The uncinate process is not developed during the first years of life, but begins to grow at the age of 6–9 years and is fully developed at the age of 18 years (*Rathke* 1933/34) Already at 4 years of age (*Hall*, 1965) and at 7 years of age (*Hirsch et al* 1967) fissures in this area were demonstrated and signs of degenerative changes are obvious at the age of 14 years These early changes may be explained by the fact that the disc and the annulus fibrosus are avascular tissues from birth (*Hirsch et al* 1967) As the disc in this area is very thin and the sliding movement in the sagittal plane is large there is a predisposition to fissure formation (*Frykholm* 1951) Changes resembling osteo arthritis are common in the unco vertebral region and according to *Krogdahl & Torgersen* (1940) they may occur without synchronous changes in other parts of the disc

Hirsch Schajowicz & Galante (1967) described the course of disc degeneration in the cervical spine on a series of 111 autopsy specimens The first stage consisted of fissures in the disc surrounded by pronounced vascularized connective tissue Then osteophytes appeared ventrally and

postero laterally. Finally, the height of the disc decreased and changes occurred in the cartilaginous endplate and the subchondral bone. Vessels infiltrated the disc which gradually was replaced by connective tissue, thus forming a fibrous anchylosis between the vertebral bodies.

The degenerative changes become more severe with increasing age, but sometimes grave changes can be observed in young individuals or small changes in old persons (*Silberstein* 1965). The changes in the disc appear earliest and become most pronounced in the C4-C6 interspaces (*Payne & Spillane* 1957, *Hadley* 1956, *Ecklin* 1960, *Silberstein* 1965, *Hirsch et al* 1967), where the range of motion anyhow in the sagittal plane is largest. This has been taken as a sign of mechanical factors causing or accelerating degenerative changes (*Hadley* 1949, 1956).

The degenerative changes in the intervertebral joints follow the classical pattern of osteo arthritis (*Hirsch et al* 1967). They are most common in the upper and middle portions of the cervical spine (*Holt & Yates* 1966). There is no correlation between the frequency or the degree of disc degeneration and osteophytes in the first place, and secondly of osteo arthritis in the intervertebral joints (*Payne & Spillane* 1957, *Friedenberg et al* 1959, *Hirsch et al* 1967). There is a general consensus of opinions about the total motion of the cervical spine decreasing with age (*Blanchard & Kottke* 1953, *Rossler & Schmeisser* 1957, 58, *Jones* 1960, *Leitler & Markuske* 1962, *Schoening & Hannan* 1964) and that increasing degenerative changes in the disc result in a proportionally decreased intersegmental motion (*Hadley* 1944, *Jones* 1960, *Ball & Meyers* 1964, *Fielding* 1964). On the other hand a locally reduced motion caused by degeneration or post traumatic changes in one segment results in a compensatory increase in the motion of adjacent segments (*Jones* 1960, *Fielding* 1964). Consequently disc degeneration must exist in more than one segment to affect the total motion (*Schoening & Hannan* 1964).

Osteo arthritis of the intervertebral joints could affect the range of motion, but *Schoening & Hannan* (1964) found no correlation between the range of motion and the degree of osteo arthritis or the number of engaged levels. Although the frequency and degree of osteo arthritis are highest in the upper intervertebral joints, *Jones* (1960) also found that the motion is proportionally greater in the upper part of the cervical spine when, in high ages, changes of the disc in the middle and lower parts caused impairment of mobility.

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2 synchronous recording of a motion in space of at least 21 points (7 vertebrae each with 3 points)
3 the method must not restrict the motion
4 reproducible measuring points

Of the measuring methods earlier used on specimens of the spine none fulfilled these demands The use of steel pins inserted into the vertebrae gives favourable results only if the motion occurs in one plane Simultaneous measurements of angular changes in several planes requires a large number of protractors fitted to the specimen which may result in restricted motion

Virchow's (1928) method of plaster impressions will cause slackness in the moulds when the specimen has been freed from the soft parts resulting in linear errors in measurement Methods involving stepped testing of the segments are adverse to the third demand

Polander's (1966) technique has the advantage of being very accurate but applied to 21 measuring points it would require a considerable number of measuring devices fixed to the specimen which would restrict the motion

Both functional radiographic examination and cineradiography are disadvantageous inasmuch as a three dimensional course is reduced to a two dimensional representation The theoretical conditions which would allow the changed positions to be measured quantitatively and with a high geometric quality on radiographs exposed in one plane only are

a that the motion occurs in one plane which is parallel with the roentgen film or that the angles to the film plane are known
b that the geometric relations between the focus object and film are known and
c that within the object to be measured there are well defined measuring points

The first demand excludes measurement of latero flexion and rotation in the cervical spine as latero flexion in a segment cannot occur without synchronous rotation and vice versa Theoretically the motion in the sagittal plane can be measured if its relation to the film plane is known At each exposure it is necessary to know where each vertebra to be measured is situated in the film plane—roentgen tube system For practical reasons this is of course impossible

As all examinations are based upon points selected in the contour of the vertebral body or the spinal process this means that when measuring a point it must be selected where a roentgen ray is a tangent

OWN INVESTIGATION

A Method

1 *Discussion of Measuring Methods*

Even if the motion, expressed in degrees is large within the cervical spine, the linear motion between the segments is small Assuming that *Penning's* (1968) construction of the centre of motion is correct a point at a distance of 20 mm from the centre would change its position only about 0 8 mm which *corresponds to an angular motion of 2°* Approximately 20 mm corresponds to the distance from the centre of *motion to the* anterior border of the superjacent vertebra For instance if the total range of motion in a segment is 20°, a linear error in measurement of only 0 8 mm will result in an angular error of 10 per cent

In order to get a correct idea of both the pattern and the range of motion a method with small linear errors in measurement would be desirable

The entire cervical spine moves as one unit in vivo With the exception of the upper two interspaces occiput—C1–C2 a *segment* never moves without a synchronous movement of the adjacent interspace In order to maintain as normal a condition as *possible* as well as the normal binding between the vertebrae it seemed advisable to examine the entire cervical spine undivided This meant that the synchronous motion of six interspaces i e seven vertebrae had to be recorded

Preliminary experiments revealed that a motion cannot be brought about which in the entire cervical spine is limited to one plane Assuming *that each vertebra is a rigid body its position in space can be determined* by means of a plane through the vertebra The position of the plane is determined by three points in the plane which are not in line and which can be reproduced in every position

In a deliberate direction of motion each vertebra must be able to move freely

The measuring method should thus cover the following demands

1 small *linear errors in measurement*

2 synchronous recording of a motion in space of at least 21 points (7 vertebrae each with 3 points)
3 the method must not restrict the motion
4 reproducible measuring points

Of the measuring methods earlier used on specimens of the spine none fulfilled these demands The use of steel pins inserted into the vertebrae gives favourable results only if the motion occurs in one plane Simultaneous measurements of angular changes in several planes requires a large number of protractors fitted to the specimen which may result in restricted motion

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to the vertebral surface The vertebral body is demarcated by irregular surfaces If a roentgen ray should be a tangent to a surface in the same point at different exposures, this means that the vertebra always should be in the same position in relation to the film and the focus of the roentgen tube As the vertebrae move relative to each other, the tangent can strike only one vertebra in the same point while the others have changed their position in relation to the roentgen ray If as a point of measurement the tip of the spinal process is used which in most of the cervical vertebrae is double it is impossible to know which of the tips forms the contour

This method is, consequently impossible to use for accurate measurements of motion, as the numerous sources of error are uncontrollable

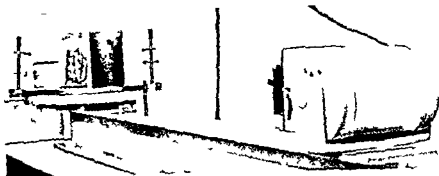
Buetti Bauml (1954) illustrated this in practice by finding that the sagittal diameter of one and the same vertebra is not always equally long when measuring different roentgen films despite identical technical conditions Furthermore when studying the published diagrams of motion (*Dittmar* 1931) and the radiographs (*Penning*, 1968) it was found that the contour of a vertebra has not the same shape in different positions

Despite this, the above method seems to be the most favourable, so far, for assessment of the intersegmental range of motion in clinical use as long as the sources of error are borne in mind, and an error of measurement of 2 is not stated at the same time as the range of motion is indicated in tenths of a degree

The method selected offers a three dimensional radiographic examination at which fixed measuring points have been created by placing small steel balls in each vertebra

2 *Apparatus*

On an approximately 2 5 m long stand consisting of an I beam 20×20 cm an object table and a roentgen tube are fitted (Fig 1) The object table (*A*) is circular and rotatable around a vertical axis which runs through a reference point (*R*) which is a steel ball with a diameter of 0 8 mm and placed in a pillar of plexiglass The object table can be locked in seven pre set positions middle position (pos 0) at 30° 22 5° and 15° each way, calculated from the middle position For this investigation only the positions +22 5° (pos I) and −22 5° (pos II) were used Perpendicular to the rotation plane of the object table there is a roentgen film holder (*B*) behind the reference point The holder which is intended for a film size of 24×30 cm can be parallelly displaced along an L square ruler (*C*) The front of the holder consists of a per



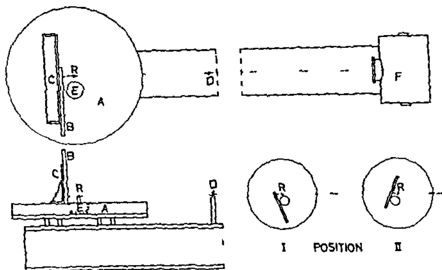


Fig 1 The apparatus For description see text

forated surface ground sheet steel and the roentgen film is fixed flat to this by means of partial vacuum (80 mm H_2O) achieved by a suction device

In the object table and in front of the film holder there is a cavity into which a brass cup (E) can be placed and secured

On the stand between the roentgen tube and the object table there is a metal rod (D) through the top of which a bore was made The rod is placed so that a line drawn through the centre of the bore and the centre of the reference point is parallel with the rotation plane of the object table and thus perpendicular to its axis of rotation and to the film plane in position 0

A

B

Fig 2 Object table with mounted specimen in position I (2A) and position II (2B) Views seen from focus of roentgen tube

The roentgen tube is a standard model Siemens Monodor SP 90/3/20 focus 0 6 mm The attachment of the tube on the stand permits adjustment in all directions and locking in the desired position Before measuring the tube is fixed so that the reference point is projected in the centre of the projected bore on the roentgen film This means that a roentgen beam (interrupted line) from the focus through the reference point strikes the film in position 0 perpendicularly and is at right angles to the axis of rotation of the object table

When examining the specimen which is fixed to the brass cup the object table is first turned to position I (Fig 2A) the film holder is moved to the left and the left part of the film is covered with a roentgen opaque shield and the first exposure can be made Then the object table is turned to position II (Fig 2B) the film holder is displaced parallel to the right and the right part of the film is covered ready for the second exposure Between the exposures the position of the specimen and the position of the film on the holder must not be disturbed

3 *Geometry*

The zero point in the primary right angled coordinate system is the reference point (*P*) The *x* axis is parallel with the roentgen film and the rotation plane of the object table in a positive direction to the left The *y* axis coincides with the rotation axis of the object table in a positive direction upwards The *z* axis is consequently at right angles to the film and parallel with the rotation plane of the table and coincides in position 0 with the central beam of the roentgen tube and is positive in the direction towards the focus of the tube The coordinate system follows the rotation of the table (Fig 3)

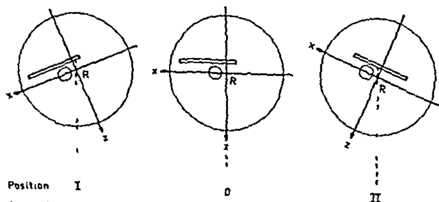
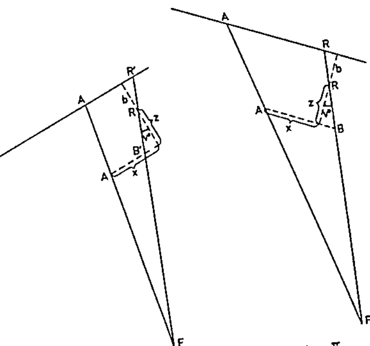


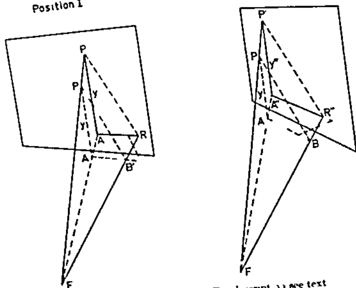
Fig 3 Rotation of primary coordinate system with the object table Dashed line runs towards focus of roentgen tube

A

B

Fig. 2 Object table with mounted specimen in position I (A) and position II (B). Views seen from focus of roentgen tube





F g 4 Geometry of the pper tus For d script n see text

Fig. 4 depicts the following geometrical conditions: P is a point in the specimen whose x, y and z coordinates are searched. P' is the picture of P on the film in position I (P'' in position II). R' (R'' respectively) is the picture of the reference point. A is the projection of P in the xz plane and F is the focus of the roentgen tube. V is the angle of rotation from position 0.

In position I the PBA plane in the pyramid $FP'R'A'$ is parallel with the base $P'R'A'$. Thus the triangle $FA'R'$ is uniform with the triangle FAB and the triangle $P'R'A'$ is uniform with the triangle PBA.

$$\frac{FR'}{FB}=\frac{A'R'}{AB}=\frac{P'A'}{PA} \tag{1}$$

The same reasoning is applied to position II and gives

$$\frac{FR''}{FB}=\frac{A''R''}{AB}=\frac{P''A''}{PA} \tag{2}$$

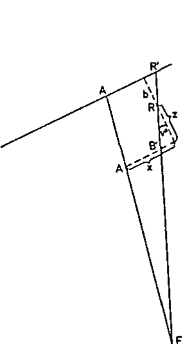
The distances $A'R'$ and $A''R''$ expressed x' and x'' and the distances $P'A'$ and $P''A''$ expressed y' and y'' are measured on the film. The distance from the reference point to the film plane is 50 mm (in the formula b mm) and the distance focus—reference point (FR) is 2000 mm (a mm). The angle of torsion, v, is 22.5°.

By using these values in the formulae (1) and (2) the following equations are obtained:

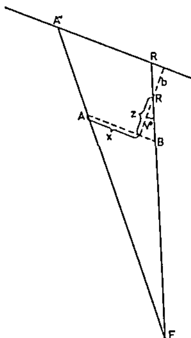
$$\frac{a+\frac{b}{\cos \iota}}{a-\frac{z}{\cos \iota}}=\frac{x}{x-z\tan v}=\frac{y'}{y} \tag{3}$$

$$\frac{a+\frac{b}{\cos v}}{a-\frac{z}{\cos v}}=\frac{x}{x+z\tan \iota}=\frac{y''}{y} \tag{4}$$

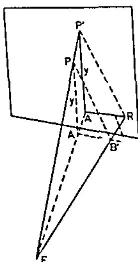
From the formulae it is seen that $y'=y''$. If this is not the case the film has been moved on its holder or the specimen has been disturbed when shifting from position I to position II. Consequently there is a control when measuring each film.



Position I



Position II



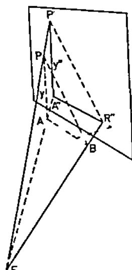


Fig. 4 Geometry of the apparatus. For description see text

Fig 4 depicts the following geometrical conditions P is a point in the specimen, whose x y and z coordinates are searched P is the picture of P on the film in position I (P'' in position II) R (R'' respectively) is the picture of the reference point A is the projection of P in the xz plane and F is the focus of the roentgen tube I is the angle of rotation from position 0

In position I the $PB'A$ plane in the pyramid $FP'R\,A'$ is parallel with the base $P\,R'A$ Thus, the triangle $FA\,R$ is uniform with the triangle FAB and the triangle $P\,R\,A'$ is uniform with the triangle $PB\,A$

$$\frac{FR}{FB}=\frac{A\,R}{AB}=\frac{P\,A}{PA} \tag{1}$$

The same reasoning is applied to position II and gives

$$\frac{FR''}{FB}=\frac{A\,R''}{AB''}=\frac{P\,A''}{PA} \tag{2}$$

The distances $A\,R'$ and $A''R''$, expressed x and x and the distances $P\,A'$ and $P''A''$ expressed y' and y'' are measured on the film The distance from the reference point to the film plane is 50 mm (in the formula b mm) and the distance focus—reference point (FR) is 2000 mm (a mm) The angle of torsion v is 22 5°

By using these values in the formulae (1) and (2) the following equations are obtained

$$\frac{a+\dfrac{b}{\cos i}}{a-\dfrac{z}{\cos i}}=\frac{x}{x-z\tan i}=\frac{y}{y} \tag{3}$$

$$\frac{a+\dfrac{b}{\cos i}}{a-\dfrac{z}{\cos i}}=\frac{x''}{x+z\tan v}=\frac{y}{y} \tag{4}$$

From the formulae it is seen that $y=y$ If this is not the case the film has been moved on its holder or the specimen has been disturbed when shifting from position I to position II Consequently there is a control when measuring each film



Position II

Position I

4A

R

y y

x

Fig. 6. Top view: Measuring points indicated on radiograph. Bottom view: Sketch of same radiograph where measured distances are indicated. N.B. $y = y'$

Treatment of Primary Data

In the first place the primary measuring values x, x' and y (y') are inserted in the formulae (3) and (4) from which the coordinates of each measuring point are obtained.

In the continued treatment it is assumed that each vertebra is a rigid body. In order to check that this is true the angles between the

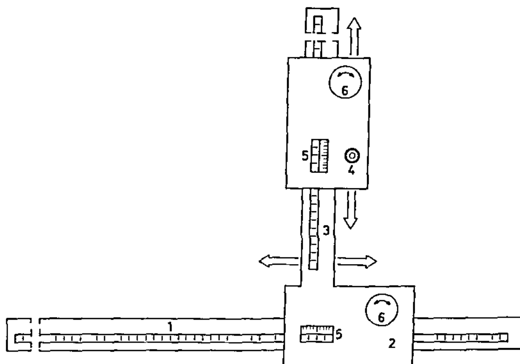
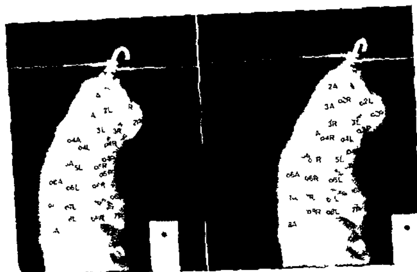


Fig 5 Detail coordinatograph Along an x ruler (1) a metal slide (2) runs to which a y ruler (3) is attached perpendicular to the x ruler Along the y ruler another metal slide runs equipped with an ocular (4) The rulers are graded The metal plates have vernier scales (5) permitting readings of $\pm 0\ 05$ mm Knobs (6) are used for moving the slides The measuring point is adjusted in the ocular ring and the x and y values can be read The arrows indicate directions of motion

4 *Measuring on Radiographs*

The film is fixed with tape against a flat horizontal glass plate which is transilluminated from below The measurings are performed by the use of a detail coordinatograph (Fig 5) the x ruler of which is placed parallel with the line $R\ R$ and the values of points R and R are noted The height adjustment is checked during the entire measuring procedure by ensuring that y and y'' are equal in each point After all the points have been measured it is made sure that the instrument has not been displaced laterally by re measuring R and R Part of the series was measured by the aid of a stereoautograph The instrument used as a monocomparator automatically records the measuring values and produces a punch tape which can be used for data processing In principle the measurements have been made in the same way and the time gained was considerable The distances measured on each film are shown in Fig 6



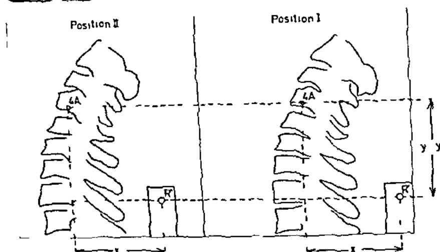


Fig 6 Top view Measuring points marked on radiograph Bottom view Sketch of same radiograph where measured distances are indicated N B $y' = y$

Treatment of Primary Data

In the first place the primary measuring values x x' and y (y') are inserted in the formulae (3) and (4) from which the coordinates of each measuring point are obtained

In the continued treatment it is assumed that each vertebra is a rigid body In order to check that this is true the angles between the

planes formed by the inserted four measuring points are calculated within each vertebra after each movement These planes are *ARP* and *ALP* and further *RLA* and *RLP* If these control angles remain unchanged, this means that the vertebra is not deformed beyond the limits of error of the method This is also a control that the primary measuring values are not erroneous, for instance by incorrect notes, erroneous punching or *mixing of the measuring points*

The cervical vertebrae are often asymmetrical and asymmetrically placed Thus, the primary measuring points cannot be symmetrically arranged In order to obtain a symmetrical and comparable neutral position, and to facilitate the study of the motion, four fictive secondary measuring points were assumed in each vertebra at the neutral position (see below) These were selected so that the *A* and *P* points lay in the *xy* plane of the primary coordinate system, and on a line forming the projection in this plane of the line between the primary points *A* and *P* The secondary *measuring point A is the projection of the primary measuring point A* in the *xy* plane, and the distance between the secondary measuring points *A* and *P* was selected to be 40 0 mm The secondary measuring points *R* and *L* form the end points of a line, 40 0 mm long the centre point of which divides the *AP* line equally and is parallel with the *z* axis of the primary coordinate system Thus the four secondary measuring points form the end points of two 40 0 mm long vectors at right angles to each other, which lie in a plane with the same inclination towards the *xz* plane as the line between the primary *A* and *P* points

After each movement the position of the secondary measuring points was calculated so that it remained unchanged in relation to the primary measuring points within each vertebra

As the purpose was to illustrate the intersegmental motion a secondary coordinate system was placed in each vertebra, using the two described vectors as two of the axes In this coordinate system the secondary measuring points of the superjacent vertebra were calculated, thus obtaining their motion in relation to the subjacent vertebra (Fig 7) These sterometric calculations mean a large number of mathematical operations which have been performed by means of data processing

6 *Preparation of Specimen and Testing*

According to *Hirsch & Galante* (1967) *Galante* (1967) and *Tkaczuk* (1968) the tensile properties of the annulus fibrosus and the longitudinal ligaments change if they are subjected to dehydration This occurs if

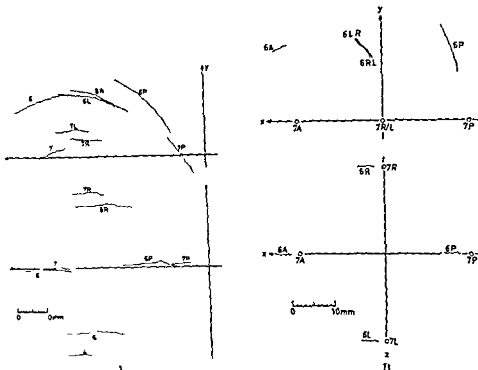


Fig Motion in a segment illustrated using primary measuring points (A) using secondary measuring points (B) transformed into the secondary coordinate system

they are not stored in an atmosphere close to a relative humidity of 100 per cent

In order to protect the specimens in this investigation against dehydration they were always stored in air tight plastic bags The specimens were always treated at room temperature (approx 22 C) and very close to 100 per cent RH

The specimen consisting of an undivided spine from C2 up to and including Th2 or 3 was freed from musculature and other soft parts only so much that the necessary anatomical details could be identified All the ligaments joint capsule and bone structures were maintained and as a further protection against dehydration a thin layer of musculature was left

In each vertebra (C2–Th1) four steel balls (⌀ 0 8 mm) were inserted The anterior (A) and the posterior (P) were inserted as closely to the sagittal plane as possible and immediately subcortically in the anterior

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the ball However as the focus of the roentgen tube is a surface partial shading of varying dimensions caused a diffuse image of the ball Thus the centre of the ball did not correspond to the centre of its image However a calculation of the discrepancy showed that it did not exceed 0 01 *mm* within the area to be *measured* As the *linear measuring results* were not indicated with more than one decimal of a millimeter this error was insignificant

The geometric formulae (3) and (4) are based on the fact that parts of the apparatus which form the primary coordinate system are at right angles to each other Within reasonable economical limits this was achieved so that the angular error in no case exceeded one minute of arc The error of angle of rotation was max $\pm 0\ 5$ These minor errors do not affect the first decimal in the result

The distance focus—reference point (*a* in the formulae 3 and 4) is 2000 mm (max error ± 2 mm) and the distance between the reference point and the film plane (*b* in the formulae 3 and 4) is 50 *mm* (max error ± 0 mm)

Primary data The measuring values x x and y (y) are dependent on the dimensional stability of the film and the error in the measuring instrument

The roentgen film was made of polyester the coefficient of expansion of which was for the temperature cm/cm/ C $= 3\ 61 \times 10^{-5}$ and for relative humidity cm/cm/$\%$ PH $= 1\ 0 \times 10^{-5}$

It has not been possible to control these factors The temperature and relative humidity were recorded however and the difference between the exposure and the measuring never exceeded 4 C and 40% PH The longest distance measured on any of the films was 280 mm The linear error of measurement depending on the dimensional instability of the film was calculated to be maximum $\pm 0\ 1$ mm under the most unfavourable conditions

The measuring error of the detail coordinatograph was max $\pm 0\ 05$ mm

In order to get an idea as to the *importance* of these *sources of error* and the mathematical procedure *from the* practical point of view a plexiglass model was made with 28 *inserted stainless* steel balls The model was radiographed and the primary data treated according to the same system as used for the *specimens*

Eight exposures were performed with the *model* placed in various positions in front of the *film* From the coordinates of the 28 primary measuring points 14 distances were derived the true lengths of which

surface of the vertebral body and the spinal process respectively The two lateral balls (R and L) were inserted in the caudal intervertebral joint processes

In the longitudinal axis of the dens epistrophei, a screw was inserted the shaft of which resembles a hook Through the vertebral body of C2 immediately below the cranial intervertebral joint surface a transversal bore was drilled through which a Kirschner wire could be inserted

The two bottom vertebrae of the specimen were fixed in the brass cup (Fig 1 E) with Plastic Padding—unsaturated polyester resin—(*Hirsch* 1964) which was inserted into the cavity of the object table One frontal and one lateral view were exposed in order to check the positions of the indicator balls Then the cup was fixed so that the sagittal plane of the specimen would coincide as closely as possible with the xy plane of the primary coordinate system The specimen was now in a resting position and was not affected by any loading One view, the neutral position, was exposed according to the earlier description

By means of thin metal wires attached to the screw in the top of the specimen and adjustably fixed to lever arms in the periphery of the object table the specimen was drawn backwards into extreme extension From this point the entire motion was performed into extreme flexion in ten steps One exposure was made between each step The motion was then reversed in the same way Consequently the motion in the sagittal plane was divided into 19 steps

The base of the specimen was rotated 90° and latero flexion was performed from the extreme left to the extreme right and back in 13 steps In the transverse bore in C2 a Kirschner wire was inserted and via a clamp which allowed free play up and down the specimen was rotated vertically The rotation was performed from extreme left to extreme right in seven steps

A total of 40 radiographs were thus obtained each having 58 measurable points i e 2300 points per specimen

7 *Discussion of Method*

The following sources of error exist

The apparatus The projection of each ball strikes the film at an oblique angle which means that the view of the ball will be elliptic If the source of radiation were a point the view of the ball would be sharply demarcated and its centre would correspond to the centre of

the ball. However, as the focus of the roentgen tube is a surface, partial shading of varying dimensions caused a diffuse image of the ball. Thus the centre of the ball did not correspond to the centre of its image. However, a calculation of the discrepancy showed that it did not exceed 0.01 mm within the area to be measured. As the linear measuring results were not indicated with more than one decimal of a millimeter, this error was insignificant.

The geometric formulae (3) and (4) are based on the fact that parts of the apparatus which form the primary coordinate system are at right angles to each other. Within reasonable economical limits this was achieved so that the angular error in no case exceeded one minute of arc. The error of angle of rotation was max. ± 0.5. *These minor errors* do not affect the first decimal in the result.

The distance focus—reference point (a in the formulae 3 and 4) is [illegible]000 mm (max. error ± 2 mm) and the distance between the reference point and the film plane (b in the formulae 3 and 4) is [illegible]0 mm (max. error ± 0.5 mm).

Primary data. The measuring values x (x') and y (y') are dependent on the dimensional stability of the film and the error in the measuring instrument.

The roentgen film was made of polyester, the coefficient of expansion of which was for the temperature cm/cm/°C $= 3.61 \times 10^{-5}$ and for relative humidity cm/cm/% RH $= 1.0 \times 10^{-5}$.

It has not been possible to control these factors. The temperature and relative humidity were recorded, however, and the difference between the exposure and the measuring never exceeded 4° C and 40% RH. The longest distance measured on any of the *films* was [illegible]80 mm. The linear error of measurement depending on the dimensional instability of the film was calculated to be maximum ± 0.1 mm under the most unfavourable conditions.

The measuring error of the detail coordinatograph was max. ± 0.0[illegible] mm.

In order to get an idea as to the *importance* of these sources of *error* and the mathematical procedure from the practical *point of view* a plexiglass model was made with 28 inserted stainless steel balls. The model was radiographed and the primary data treated *according* to the same system as used for the specimens.

Eight exposures were *performed* with the model placed *in* various positions in front of the film. From the coordinates of the 28 primary measuring points 14 distances were derived, the true lengths of which

were unknown Of the eight values obtained for each distance a calculation was made for the mean, the standard error of the mean (s e m) and the standard deviation (S D) Of the 14 values obtained of s e m and S D a calculation was made for the mean and S D (Table 2)

Table 2

	N	Mean	S e m	S D
Standard deviation	14	0 083	0 000	0 036

If the variations in S D are used to find the reproducibility of the length determinations, the mean reproducibility will be 0 08 This means that the error of the measuring method with respect to the apparatus and the two primary geometrical formulae was less than 1/10 mm The mean of the distances measured was 47 2 mm which gave a standard deviation of 0 2 per cent of the mean distance

The same 14 distances were calculated on the coordinates of the same points in the secondary coordinate system According to the definition all these distances should be 40 0 mm The mean of the 112 distances was 39 98 mm (s e m 0 1 mm S D 0 9 mm) The deviation from 40 0 mm was not significant The standard deviation of the whole procedure including all the geometrical calculations was thus 0 9 mm or 2 25 per cent of the defined distance

B Material

1 *Selection and Age Distribution*

The investigation included 28 cervical spines which were obtained from the Departments of Pathology University City Hospital Gothenburg

The specimens were removed with surrounding musculature and immediately placed in plastic bags If the examination could not be performed at once the specimen was stored in a deep freeze refrigerator at $-25°C$ but were thawed to room temperature before testing

The specimens were selected to a certain extent Specimens from patients who had died in malignant diseases were avoided Furthermore all the specimens were rejected which on preparation or radiographic examination showed signs of other changes than degenerative This meant that cervical spines with post traumatic changes of the type luxations or subluxations were excluded

Much care was taken to avoid damaging the bone structures joint capsules or ligaments when collecting or preparing the specimens If any lesion of this type was revealed the specimen was rejected

Age sex and cause of death are tabulated (Table 3) The age of the deceased ranged from 11 to 67 years (mean age 52 0 years) Half of the series belonged to the age group 40–60 years

2 Classification of Degenerative Changes

In order to correlate the variation in the pattern and the range of motion to degenerative changes roentgenographic and macroscopic assessments were made

Table 3

Spec No	Age years	Sex	Cause of Death
1	11	F	Cerebral ischaemia
[illegible]	[illegible]	M	Bronchopneumonia
3	34	M	Cerebral tumor + circulatory failure
4	38	M	Pneumonia
5	46	F	Uraemia
6	48	F	Intracranial art an ury m with haemorrhage
[illegible]	4[illegible]	M	Cirrhosis of the liver
8	4[illegible]	F	Aneurysm of basilary artery
[illegible]	48	F	Gastrointestinal bleeding
10	48	M	Circulatory failure
11	[illegible]	F	Myocardial infarction
1[illegible]	51	M	Myocardial infarction
13	[illegible]	M	Pneumonia
14	[illegible]	M	Cerebral thrombosis
1[illegible]	[illegible]	M	Gastrointestinal bleeding
16	[illegible]	F	Intracerebral bleeding
[illegible]	[illegible]	M	Pulmonary embolism
18	[illegible]	F	Myocardial infarction
1[illegible]	6[illegible]	M	Cerebral haemorrhage
[illegible]	[illegible]	M	Respiratory and circulatory failure
[illegible]	[illegible]	M	Myocardial infarction
[illegible]	[illegible]	M	Respiratory failure
[illegible]	[illegible]	F	Myocardial infarction
[illegible]	[illegible]	F	Peritonitis
[illegible]	[illegible]	M	Peritonitis
[illegible]	[illegible]	M	Myocardial infarction
[illegible]	[illegible]	F	M Sternberg circulatory failure
[illegible]	[illegible]	F	Cerebral tumor + circulatory failure

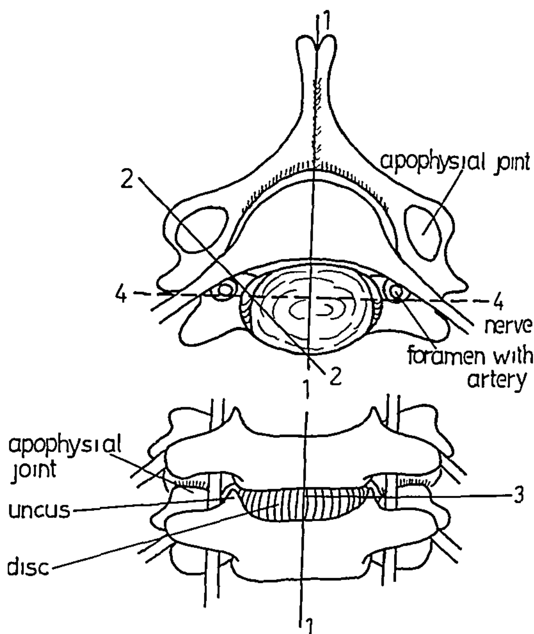


Fig 8 Sketch showing how the specimens were cut (*Hirsch et al* 1967 Repr with permission of authors)

The roentgenological changes were studied on the frontal and lateral views and on oblique views on which the specimen had been rotated 22 5° in either direction from the frontal view The two latter projections gave a good view of the intervertebral joints

Tal le 4 Gra ling of D gen ratwe Changes

Grade	Disc	Intervertebral Joint
	Macroscop ic cl anges	
0	Normal disc Sh ny white annulus an l nu l u Di t nct border betwe n annul s and nucl us	Normal cartilage shiny smooth wh te
1	Lamellated f l ro is structure of annulus	Rough dry surface with small ero ons
2	Ol o is degen rati e changes n nu l us an l annul s F ssures	Pronoun ed erosion
3	Marked legeneration in both annulus and nu l us Ruptures an l sequesters up to compl te replacement of the nucl u s by f l rous tissue	Total destruction of cartilage
	Roentgen grap l c changes	
0	N rmal he gl t No osteopl yt s	Normal joint pace no osteophytes
1	Sl ght red ct on of disc le l Min nal to small osteopl ytes	Sl ghtly reduced jo nt space Small osteopl yt s
2	Prono ince l redu tion of l sc l vel Mod rate o teopl ytes Sl gl t sul l on lral scl ros	Reduced jo nt space Mod rate osteopl ytes an l i regular cartilag bone b rd r
3	Pronounced t total re l ction of l sc l l Larg osteopl yte	Large osteophytes to roentgenologic an l ylos

For the macroscopic evaluation the specimens were cut according to the principles stated by *Hirsch et al* (1967) An approximately 4 mm thick slab was cut from the sagittal plane of the entire specimen (Fig 8 1) One of the halves was cut in the horizontal plane of each disc (Fig 8 3) and the other vertically through the uncus region (Fig 8 2) Each di c thus was divided so that a cross section through one half a section of its sagittal extension and an oblique section through the other half were obtained The cuts of the two specimen halves passed through the intervertebral joints on either side which could easily be opened allowing the joint cartilage to be examined

The macroscopic asses ment was concentrated on the condition of the di c and the joint cartilage and the roentgenologic on the adjacent bone structure

The condition of the disc was evaluated according to statements on lumbar discs made by *Friberg & Hirsch* (1949 50) and *Hirsch & Schajo-* ic (19)

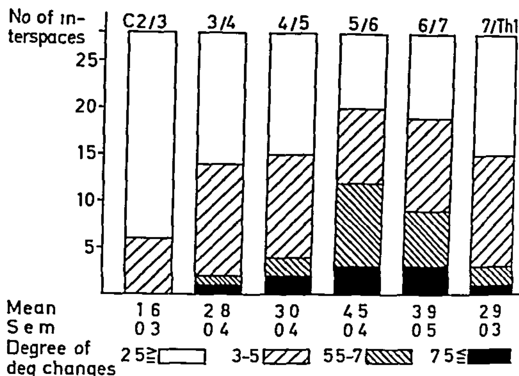


Fig 9 Distribution of degenerative changes

The limits between the various degrees as illustrated in Table 4 are indistinct but the purpose was not to give a detailed description of the degenerative changes but instead to obtain a relative grading

According to the table each disc and each intervertebral joint can receive 0–6 points To prevent the degenerative changes of the intervertebral joints from being exaggerated in relation to the disc the total of the two joints of each interspace was divided by two By adding the points of the disc and the joints each interspace may receive 0–12 points The distribution of the degenerative changes on various segments is given in Fig 9

The figure shows that in the C5/6 interspace most of the degenerative changes were found and that they decreased gradually with the distance from that interspace

In order to check that the series similar to earlier investigations showed increasing degeneration with increasing ages (*Silberstein* 1965 *Hirsch et al* 1967) and that the grading and the evaluation were correct a *T* test was performed The specimens were divided into two groups

each including 14 one with ages ranging from 11–53 years the other from 55–67 years The degree of degeneration was compared in each inter space and in the entire specimen The latter age group revealed at the 5% level significantly increasing degenerative changes in all the inter spaces and in the entire specimen

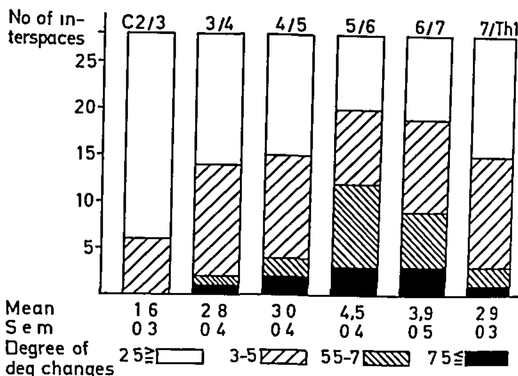


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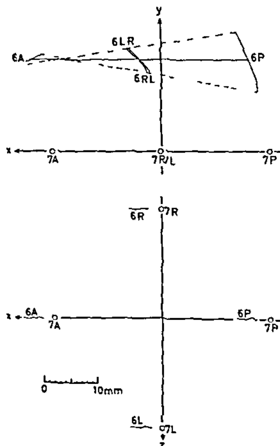


Fig. 10. Curves of motion of measuring points in r[illegible]t[illegible]on and l[illegible] fl[illegible] [illegible] in the xy plane (top) and the xz plane (bottom). [illegible] dashed line indicates extreme flexion, dashed line indicates extreme extension, solid line neutral position.

(Fig. 11). Two diagrams were obtained of the latero flexion, one for the motion from the extreme right to the extreme left side and one for the reverse motion.

All the ranges of motion were indicated in angles and in relation to the neutral position of each vertebra. For calculation of the angles the coordinates were used for the extreme positions of the measuring points. At motion in the sagittal plane the A and I points were projected in the sagittal plane of the vertebra. At latero flexion the J and I points were projected in the frontal plane (Fig. 1A) and at rotation in the horizontal

RESULTS

A General Remarks

The results are based on approximately 100 000 primary measuring values, which after data processing resulted in x, y and z coordinates for approximately 35 000 measuring points and the earlier described control angles

These angles are calculated in all exposures and for the same vertebra vary only within a few tenths of a degree Singular deviations above this limit are very large and obviously depend on error when measuring the radiograph or when punching the results When a large deviation was found the result of this exposure was rejected If any vertebra was deformed under load it seems reasonable to believe that the deformation is largest in the position where the specimen was subjected to the heaviest force i e in the extreme positions of the movements As a control the angles in the neutral position and in the eight extreme positions were chosen in seven random selected specimens In each vertebra the mean, the s e m and the S D for these nine pairs of angles were calculated Of the 98 values obtained for the s e m and the S D the mean, the s e m and the S D were calculated and compared with the values obtained in the same way for all the control angles of the plexiglass model The differences are not statistically significant and therefore it can be assumed that the vertebrae were not deformed outside the error of the method Thus in the following they can be regarded as rigid bodies

The secondary coordinate system was drawn on transparent paper The measuring points were inserted and their stepwise movements were indicated In this way a diagram of motion was obtained

The motion in the sagittal plane was plotted in the xy plane (lateral view of the vertebra) and the xz plane (the vertebra seen from above) of the secondary coordinate system (Fig 10) Two diagrams were obtained, one for the motion from extreme extension to extreme flexion and one for the reverse motion

The latero flexion and the rotation were plotted in the yz plane (front view of the vertebra) and the xz plane of the coordinate system

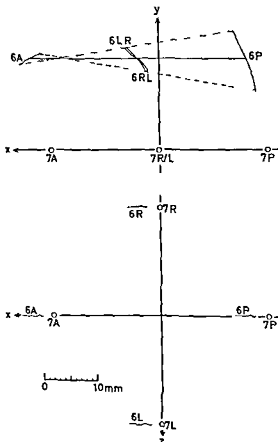


Fig 10 Course of motion of measuring points in extension and flexion traced in the xy plane (top) and the xz plane Pointed dashed line indicates extreme flexion dashed line indicates extreme extension solid line neutral position

(Fig 11) Two diagrams were obtained of the latero flexion one for the motion from the extreme right to the extreme left side and one for the reverse motion

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Fig. 1 A. Frontal axis in neutral position (R–L) and after motion (P–L) and projections in frontal plane of P and L. V is the calculated angle at latero flexion

proved that the pattern of motion was independent of the direction of motion

In all the interspaces examined the extension was a combination of backwards tilting and backwards sliding The flexion was a combination of forwards tilting and forwards sliding All the points in the vertebra moved parallel to the sagittal plane (Fig 13) Due to this the centre of the motion must be an axis which is parallel to the frontal plane and situated in or under the vertebra

If this axis is fixed the course of each measuring point should constitute part of a circle If the course of each measuring point is rectilinear this means that the axis of motion moves In order to find the centre of motion von Euler's principle was employed If a rigid body moves in one plane the centre of motion can be determined as the intersection between the mean centre proportionals of two lines connecting the

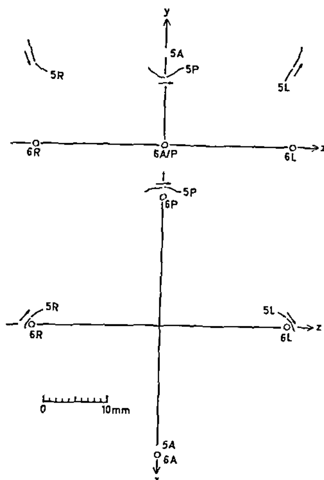


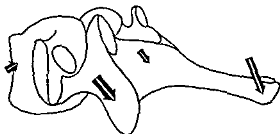
Fig 11 Course of motion of measuring points in latero flexion and rotation traced in y plane (top) and xz plane Interruption in the courses indicates neutral position Arrows indicate direction of motion from left to right latero flexion

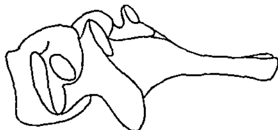
plane (*Fig 12B*) Thus the range of motion is expressed in the angle formed by the neutral position of the sagittal and the frontal axes respectively and the projection in each plane of the same axis after motion

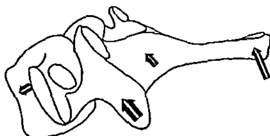
B Pattern of Motion

1 *Sagittal Plane*

The two diagrams obtained from each vertebra of the motion in the sagittal plane were compared to each other In no case of the entire series did these two diagrams of motion reveal different patterns which







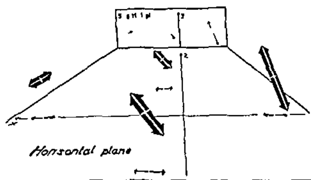


Fig 13 The pattern of motion in the sagittal plane From above extension neutral position and flexion Bottom motion projected in sagittal and horizontal planes

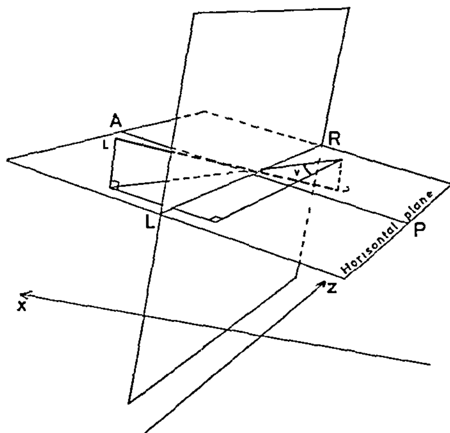


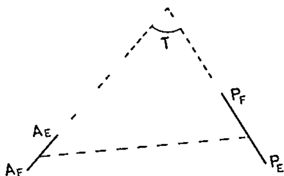
Fig 12 B P and L projected in horizontal plane and the calculated rotation angle V

respective positions of two random selected points in two phases of the motion The principle was used for each step of the motion in the sagittal plane (Fig 14) The intersections will form a straight line, regularly situated within the subjacent vertebral body In motion from extension to flexion the axis moves from below posteriorly upwards anteriorly thus towards the concave side of the motion

However a detailed study of the diagrams shows that the courses of motion usually are rectilinear but sometimes arched with the convexity towards or away from the vertebra It has been impossible to determine whether the axis of motion is fixed or moves

The distance of the axis from the vertebra decides the course of the motion The closer the centre of motion is to the vertebra the less the translation per degree of rotation thus the steeper the course

In order to obtain a relative measure of this the so called Top angle



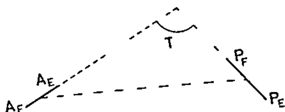


Fig 13 Construction of T angle A_E-A_F and P_E-P_F are the courses of motion of the anterior and posterior measuring point A small T angle indicates a steep course of motion (top) and a large T angle indicates a flat course (bottom)

Table 5

Paired comparison of the Top angle

	C	C3	C4	C5	C6	C7
\		8	8	8	8	7
Mean	9 8	8	87 4	83 9	7 8	80
SD	3	8	7 5	8 ,	8 0	8 7

T_{diff} at comparison of vertical to horizontal values

	C	C3	C4	C	C6
C3	4 1 33				
C4	4 6	−0 0811			
C	8 6116	1 4868	1 3039		
C6	5 6	4 3 60	4 6 8	2 7 61	
C	7 990	9618 *	3 1	1 4 03	−1 19 1

P 0 0 0 01 0 001

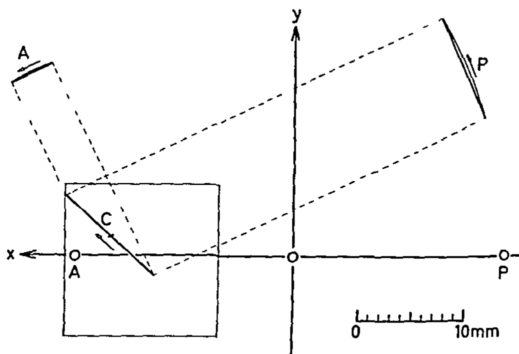


Fig 14 Centre of motion if courses of measuring points are arched (dash at *C*) or if they are rectilinear (line at *C*) Subjacent vertebral body indicated in grey

(T angle) was constructed in each vertebra as follows (Fig 15) The courses of motion of the anterior and posterior measuring points were extended in a cranial direction and the angle formed was calculated The larger the angle is the more extensive the sliding of the vertebra will be in relation to its tilt If the T angle is 180 there is no tilt if the T angle is 0° there is no sliding The mean of the T angles in the various interspaces were compared in pairs in the whole series (Table 5)

The T angle of C2 is significantly larger than that of all the other vertebrae and of C6 significantly less than that of all the others with the exception of C7 Furthermore the T angles of C3 and C4 are larger than the angle of C7

Thus the course of motion is the most flat in C2 C6 takes the steepest and C7 the next steepest course while the courses of the remaining vertebrae are uniform This means that the axis of motion of C2 is situated furthest distal to the vertebra and the axes of C6 and C7 lie closest to their respective vertebra

Table 7

Va ation of the T angle with increa ing degenerat on

	C	C3	C4	C5	C6	C7
Deg group	0 0–1 0	0 0–3 0	0 0–3 0	0 0–4 0	0 0–4 0	0 0–3 0
N	13	14	14	14	14	13
Mean	9, 9	88 0	89 1	86 7	80 0	83 1
SD	3	6 7	6 9	6	5 3	9 0
Deg group	1 5– 0	3 0–9 0	3 0–8 0	4 0–5 0	4 0–8 0	3 0– 5
N	14	14	14	14	14	14
Mean	97 6	8 5	85 7	81 1	6	78 0
SD	10 9	9	8 0	31	98	8 0
T_{diff}	+0 0837	+1 108	+1 195	+1 7831	+1 4 1	+1 5 07

Table 8

Va ation of th rat o extens on/flex on with increasing degenerat on

Vertebra C5

Deg group	0 0 –4 0	
N	14	
Mean	0 6	
SD	0 6	
Deg group	**4 0 –9 0**	
N	14	
Mean	0 7	
SD	0 6	
T_{diff}	– 10 8	P=0 0

The two diagrams of the pattern of motion in the frontal plane were compared to each other and in no case was there any difference in the pattern when the motion occurred from the right to the left as compared to the reverse direction

The motion in the frontal plane (Fig 16) is a combination of lateral tilt and rotation in the same direction i e latero flexion to the right is combined with rotation to the right (clockwise) and latero flexion to

Table 6

Paired comparison of the ratio extension/flexion

	C2	C3	C4	C5	C6	C7
N	27	28	28	28	28	27
Mean	0 55	0 67	0 61	0 66	0 77	0 80
SD	0 41	0 33	0 27	0 28	0 31	0 38

T_{diff} at comparison of vertical to horizontal values

	C2	C4
C6	−2 2592*	−2 1533*
C7	−2 2690*	−2 1480*

2P=0 05* Only significant differences shown

The ratio extension/flexion varies with each interspace (Table 6) The degree of flexion is always higher than that of extension, and the difference is most pronounced in the upper portion of the cervical spine The flexion is almost double as compared to extension in C2, while C6 and C7 reveal the relation 4 5 The individual variation however is very large and the differences are significant at the 5% level only when C2 and C4 are compared with C6 and C7

The effect of degenerative changes on the pattern of motion was examined by studying the variations in the T angle and the ratio extension/flexion

Within each interspace the values were arranged according to the increasing degree of degeneration and the least degenerated half was compared with the most degenerated

On all levels the T angle becomes reduced with increasing degeneration Thus the course of motion will be steeper with increasing degeneration The *T* test (Table 7) is not significant for any singular vertebra but as they were all reduced there is still a statistical significance at the 5% level (Sign test)

The ratio extension/flexion does not alter significantly except for C5, where with increasing degeneration the flexion becomes reduced in relation to the extension (Table 8)

2 Frontal and Horizontal Planes

The pattern of motion in these two planes are dealt with simultaneously as they are very uniform

Table 7

Variation of the T angle with increasing degeneration

	C	C3	C4	C5	C6	C
Deg group	0 0–1 0	0 0–3 0	0 0–3 0	0 0–4 0	0 0–4 0	0 0–3 0
N	13	14	14	14	14	13
Mean	9[illegible] 9	89 0	89 1	86	80 0	83 1
SD	3	6 7	6 9	6	[illegible] 3	9 0
Deg group	1 [illegible]–5 0	3 0–9 0	3 0–8 0	4 0–9 0	4 0–8 0	3 0–[illegible]
N	14	14	14	14	14	14
Mean	97 6	8	85 7	81 1	[illegible] 6	8 0
SD	10 9	9 5	8 0	[illegible] 1	8 8	8 0
T_{diff}	+0 087	+ 1 108[illegible]	+1 [illegible]195	+1 [illegible]831	+1 4[illegible]1	+1 5 07

Table 8

Variation of the ratio extension flexion with increasing degeneration

Vertebra C

Deg group	0 0–4 0	
N	14	
Mean	0 56	
SD	0 6	

Deg group	4 0–5 0	
N	14	
Mean	0 7	
SD	0 [illegible]6	
T_{diff}	– 10 8	P 0 05*

The two diagrams of the pattern of motion in the frontal plane were compared to each other and in no case was there any difference in the pattern when the motion occurred from the right to the left as compared to the reverse direction

The motion in the frontal plane (Fig 16) is a combination of lateral tilt and rotation in the same direction i e latero flexion to the right is combined with rotation to the right (clockwise) and latero flexion to

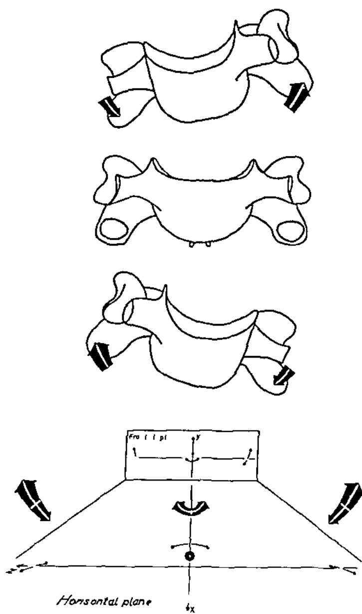


Fig 16 The pattern of motion in the frontal and horizontal planes From above latero flexion and rotation to the right neutral position and latero flexion and rotation to the left Bottom Motion projected in frontal and horizontal planes

the left is combined with rotation to the left (anti clockwise) The pattern of motion in the horizontal plane is the same as in the frontal plane

The centre of motion in both planes is situated in the sagittal plane and in the anterior contour of the vertebral body This was proved due to the position there of the anterior measuring point In fact on the diagrams of motion it is found that the anterior measuring point regularly is unmoved or has moved within a very limited space The distance covered by the *A* point from one extreme position to the other in latero flexion and in rotation was calculated for all the vertebrae The mean was 0 88 mm (s e m 0 04 S D 0 42) Thus the distance is very small and the anterior measuring point lies very closely to the centre of motion It was also found that the other measuring points described arched courses with their concavity directed towards the *A* point

The proportion between latero flexion and rotation when the specimen was latero flexed was obtained by dividing the latero flexion by rotation expressed in degrees The ratio obtained was compared in pairs (Table 9)

The rotation combined with latero flexion was proportionally largest for C2 where the ratio was 3 2 and gradually diminished downwards in the cervical spine In C7 the latero flexion was 7 5 times larger than the rotation occurring at the same time The difference is always statistically significant when a vertebra is compared with the vertebra two steps below

Table 9

I a red compar son of tl e ratio latero fl x on/rotat on wh n the spec men is latero fl xed

	C	C3	C4	C	C6	C
N	6	7	8	8	8	6
M n	1 4	1 84	1 75	61	- 3	48
SD	0 81	1	0 84	3	0 50	9

$T_{d\,ff}$ t compa son of ert cal to horizontal values

	C	C3	C4	C	CC
C3	−0 186				
C4	−1 0	+0 8			
C	− 48 0	−1 4 9	−1 9 63		
C6	− 4 4	− 34 4	−4 16	−0 14 1	
C	−3 8304	−3 300	−3 8304	−3 0 08	−3 1390*

1 = 0 0 0 01 0 001

Table 10

Paired comparison of the ratio rotation/latero flexion when the specimen is rotated

	C2	C3	C4	C5	C6	C7
N	17	22	23	23	23	22
Mean	1 14	1 59	2 09	2 17	1 92	4 00
SD	0 43	1 03	1 08	1 73	1 40	4 12

T_{diff} at comparison of vertical to horizontal values

	C2	C3	C4	C5	C6
C3	−1 6824				
C4	−3 4357**	−1 6071			
C5	−2 4084*	−1 3773	−0 1917		
C6	−2 2144*	−0 9052	+0 4622	+0 5458	
C7	−2 8432**	−2 6676*	−2 1497*	−1 9585	−2 2915*

2P=0 05* 0 01**

The ratio rotation/latero flexion when rotating the specimen was compared in the same way (Table 10)

The latero flexion combined with rotation was largest for C2 and least for C7 A comparison between the other vertebrae was not statistically significant

The effect of the degenerative changes on the pattern of motion in the frontal and horizontal planes were studied by comparing the least degenerated half of the series with the most degenerated Neither the distance of motion from one extreme position to the other covered by the *A* point nor the ratio latero flexion/rotation or rotation/latero flexion revealed any statistically significant differences in any interspace

C Range of Motion

The values reported refer to the entire series and it must be borne in mind that the series includes various degrees of degeneration The ranges of motion cannot be regarded as mean values of spines with non degenerated unaffected discs

The values of latero flexion and rotation are the total of the range to the right and to the left

Table 11

Paired comparison of the range of motion in the sagittal plane

	C	C3	C4	C5	C6	C7
N	7	8	8	8	8	7
Mean	4 9	10 2	13 0	14 5	13 5	8 0
S e m	0 4	0 5	0 7	0 6	0 8	0 4
SD		7	3	3 2	4 4	2 6

T_{diff} at comparison of vertical to horizontal values

	C	C3	C4	C5	C6
C3	−7 8 93***				
C4	−10 1511	−3 3 05			
C	−1 89 9	−5 3631***	−1 6174		
C6	−9 1/11	−3 405	−0 48	+0 9 17	
C7	−5 480 *	+3 44	+6 2/90 **	+8 74 4*	+5 8758 **

P = 0 0 0 01 0 001

1 *Sagittal Plane*

The mean of the total range of motion in the sagittal plane in this series was

Extension 24 (s e m 1 S D 6)
Flexion 40 (s e m 2 S D 8)
Total 64 (s e m 2 S D 10)

There were large individual variations

The distribution of the total range of motion within the cervical spine varied (Table 11) The range of motion was least in C2 and increased in C7 and C3 in the order mentioned The middle cervical vertebrae C4 C5 and C6 had the most equal and the largest range of motion

A comparison of the range of motion in each interspace between the most degenerated and the least degenerated half of the series did not reveal any statistically significant differences at any level neither in extension flexion nor total motion In order to control this result the series was divided into several small groups with regard to the degree of degeneration and a variance analysis was performed There were no criteria of the degree of degeneration having any effect on the range of motion

2 *Frontal Plane*

There was no difference in this series between the range of motion to the right and to the left

As the intersegmental range of motion when the specimen was latero *flexed, was related to the neutral position of each vertebra* it was not geometrically correct to add together the intersegmental ranges of motion in order to obtain the total range As the deviation was small the addition was still made and the mean values obtained

Latero flexion 49° (s e m 3° S D 14°)
Combined rotation 28° (s e m 2° S D 8°)

There were large individual variations

The intersegmental range of motion had a comparatively even distribution with the exception of C7 which moved less than the others (Table 12) The rotation combined with latero flexion was unevenly distributed in the cervical spine (Table 13) The proportional relation has been indicated in Table 9 (Page 49)

There were no statistically significant differences when the intersegmental range of motion in the least degenerated half of the series was compared with the most degenerated

3 *Horizontal Plane*

The total range of motion when the specimen was rotated was calculated in the same way as when it was latero flexed and the mean values were

Rotation 45° (s e m 5° S D 18)
Combined latero flexion 24° (s e m 3 S D 10)

Also in this plane the individual variation was very large The intersegmental distribution revealed that the range of motion was largest in C4 and least in C2 C6 and C7 (Table 14)

The mean of *the latero flexion combined with rotation* was largest in C3 and least in C7 (Table 15) The ratio has been indicated in Table 10 (Page 50)

No statistically significant differences could be demonstrated in this plane of motion either in a comparison *between less or more degenerated* interspaces

Table 1

Pa red comparison of the range of motion in the frontal plane

	C	C3	C4	C5	C(	C7
N	26	27	8	8	8	6
Mean	7 9	9 8	9 1	9 0	8 4	6 3
S.e m	0 6	0 6	0 (	0 5	0 6	0 4
SD	9	3 4	9	7	3 4	--

$T_{d\ ff}$ at comparison of ertical to horizontal values

	C	C3	C4	C5	C(
C3	− 300				
C4	−1 50 8	+0 8534			
C5	−1 4 10	+1 0087	+0 1367		
C6	−0 5941	+1 5333	+0 936	+0 604	
C7	+ 516	+4 4963	+3 9 8	+3 9717 *	+2 6746

P = 0 0 0 01 0 001 *

Table 13

Mean alues of the rotation co nbined with latero flexion when the specimen is latero flexed

	C	C3	C4	C	C6	C
M an	6 1	6 8	6 1	4 7	3 4	2 0
S e m	0 4	0 5	0 5	0 4	0 3	0 4
SD	6	8	5	3	1 8	1 8

Table 14

Pa red comparison of the range of motion in the ho ontal plane

	C	C3	C4	C5	C6	C7
N	1		3	3	3	--
M an	6 0	9 8	10 3	8 0	5 7	4 7
S e m	0 8	1 1	0 9	0 8	0 9	0 4
SD	3 4	4 9	4 1	3 9	4 3	1 9

$T_{d\ ff}$ at comparison of vert al to horizontal values

	C	C3	C4	C5	C6
C3	− 71 0				
C4	−3 5 94 *	−0 3536			
C	−1 7373	+1 3334	+1 9515		
C6	+0 1930	+2 9448 *	+3 118*	+1 90 0	
C7	+1 4400	+4 4834	+5 8 3* *	+3 9 (	+0 998

P = 0 01 0 001

Table 15

Mean values of the latero-flexion combined with rotation when the specimen is rotated

	C2	C3	C4	C5	C6	C7
Mean	5.4	6.8	5.7	4.[illegible]	4.7	[illegible]0
S.e.m.	0.7	0.8	0.7	0.6	0.5	0.4
SD	2.7	3.5	3.4	2.7	2.6	1.4

D. Conclusions and Discussion

1. *Pattern of Motion*

The patterns of motion in the cervical spine are of two entirely different types. In the sagittal plane the motion is limited to one plane, i.e. each point in a vertebra moves parallel to the sagittal plane. The motion can be described as a rotation in this plane around an immobile or mobile axis which is perpendicular to the plane.

In the frontal and the horizontal planes the motion, on the other hand, occurs in several planes, but is symmetrical in relation to the sagittal plane and, therefore, can be described as a rotation around a point in this plane.

These two types of motion are controlled by the shape of the discs and the intervertebral joints. As the system of an ideal case is symmetrical with respect to the sagittal plane, but asymmetrical with respect to the other two planes, it is reasonable to expect different patterns of motion. In principle the patterns of motion observed do not differ from those reported by other authors (cf. Review of Literature).

The axis of motion in the sagittal plane was found to lie in the subjacent vertebral body, however, on different levels in different segments. The size of the Top angle (Page 44) shows that the axis of the C2 motion lies further distal than those of C6 and C7. This finding is in accordance with *Penning's* (1968) positioning of the C2 axis of motion caudal in the C3 vertebral body and the C6 axis cranial in the C7 vertebral body. It has been impossible to decide whether the axis of motion is immobile or whether it moves.

The centre of motion in the frontal and horizontal planes proved to lie in the anterior contour of the vertebra and in the sagittal plane. The diminutive movement, less than one millimeter, made by the anterior measuring ball at motion from one extreme position to the other, for obvious reasons depends on the impossibility of placing the ball right in the centre of motion.

The position of this centre has not been mentioned in earlier literature *Bakke* (1931) however observed that a vertebra in latero flexion slides on the subjacent vertebra towards the convex side This is in good accordance with a centre of motion placed anteriorly to the joint processes the latter of which at rotation are turned forwards on the convex side and on a frontal view are projected further lateral than the processes of the subjacent vertebra

As mentioned earlier the Top angle is a measure of the shape of the course of motion in the sagittal plane The proportion between latero flexion and rotation when the specimen is latero flexed is a measure of the shape of the course of motion in the frontal and horizontal planes If latero flexion occurs without simultaneous rotation the motion is limited to one plane and the ratio is infinite (latero flexion x rotation 0 $\frac{X}{0}$ = infinity) If the latero flexion and the rotation are equal there will be equal motion in both planes and the ratio will be 1 The same reasoning can be applied to the ratio rotation/latero flexion when the specimen is rotated

C2 has the largest Top angle and at the same time the lowest ratio of latero flexion/rotation and rotation/latero flexion This means that C2 at the same time has the most flat course of motion in the sagittal plane the largest rotation combined with latero flexion and the largest latero flexion combined with rotation There is a complete reverse condition for C7

The tendency for the vertebrae lying in between even if it is not statistically significant in all details is that the T angle becomes reduced and the two ratios increase gradually down the cervical spine

The above statement can be regarded as a proof that the *freedom* of motion found in a vertebra as related to the subjacent one is largest in the upper portion of the cervical spine and becomes reduced in a distal direction It was also found that the flexion proportionally was the largest in C2 and became reduced in a distal direction

Degenerative changes affect the pattern of motion only with respect to the course in the sagittal plane and the proportion between extension and flexion in the interspace of C5/6

The course of motion is statistically significant steeper with increasing degeneration and in analogy with the above statements this implies that the freedom of motion of the vertebrae in relation to the subjacent one becomes reduced with increasing degeneration

The fact that the flexion was reduced in relation to the extension

only in C5 may depend on the most pronounced changes in the series being found there

2 *Range of Motion*

There were large individual variations in all directions of the range of motion in the cervical spine

The means of the intersegmental range of motion in the sagittal plane and at latero flexion lie within the limits found on earlier studies of specimens but at rotation the mean is lower

In the sagittal and the horizontal planes, the intersegmental range of motion is largest in the middle parts of the cervical spine, while the motion in the frontal plane is more evenly distributed

Contrary to most of the earlier investigations there is no correlation between reducing range of motion and increasing degeneration This applies to all directions of motion, to all interspaces and also to the total motion of the specimens

Galante (1967) stated regarding the annulus fibrosis in the lumbar spine that after the middle of the third decade no significant changes in tensile properties were present as a function of aging'

It is true that *Galante s* results deal with the lumbar spine, but if his findings can be applied to the cervical spine this may partly explain why the range of motion is not affected by degenerative changes in the present series in which all specimens except two were obtained from deceased persons older than 30 years

Furthermore *Hirsch & Lewin* (1968) when studying the range of motion in the lumbo sacral synovial joints found that disc degeneration did not affect the excursion of the L5 facet relative to the sacrum

However, it is not sure that changes in the morphology of the disc and the intervertebral joints cause a reduction of the range of motion *Schoening & Hannan* (1964) measured the total range of motion of the cervical spine in living subjects by means of a 17" wand firmly fixed to the occiput Even if the method has large sources of error there was no correlation between the range of motion in the first place and inter space narrowing in one level posterior bar or apophyseal arthritis on one or many levels in the second place Contrary to this pain in the neck, arms and upper trunk tenderness over the articular masses and spinal processes pain with passive neck motion or increased muscularity caused reduced range of motion

SUMMARY

The primary intention was to demonstrate the intersegmental pattern of motion in the cervical spine and therefore an apparatus for three dimensional radiographic examination of autopsy specimens was designed

The series consisted of 28 autopsy specimens including C3–Th1 in the age groups 11–67 years The specimens were indicated with steel balls and tested for the pattern of motion in the sagittal frontal and horizontal planes The motion in each plane was represented by a number of stepped movements

After data processing including a number of geometrical transformations motion diagrams were drawn

The motion in extension flexion was parallel to the sagittal plane and made its course around an axis in the subjacent vertebral body perpendicular to this plane The appearance of the course varied between the different interspaces Increasing degenerative changes affected the pattern of motion in the sagittal plane so that the freedom of motion between the vertebrae was reduced

The patterns of motion in latero flexion and rotation were similar to each other One movement is always combined with the other and there is only a difference in the proportion between latero flexion and rotation when the specimen is latero flexed or rotated The centre of motion is a point situated in the anterior contour of the body of the moving vertebra and in the sagittal plane The pattern of motion in the frontal and horizontal planes were not affected by degenerative changes

The maximum ranges of motion in all planes were calculated and the results lay within the limits earlier found on examinations of specimens except for the rotation which in this series was lower

Degenerative changes had no effect on the range of motion in any planes or in any interspaces

only in C5 may depend on the most pronounced changes in the series being found there

2 *Range of Motion*

There were large individual variations in all directions of the range of motion in the cervical spine

The means of the intersegmental range of motion in the sagittal plane and at latero flexion lie within the limits found on earlier studies of specimens but at rotation the mean is lower

In the sagittal and the horizontal planes the intersegmental range of motion is largest in the middle parts of the cervical spine while the motion in the frontal plane is more evenly distributed

Contrary to most of the earlier investigations there is no correlation between reducing range of motion and increasing degeneration This applies to all directions of motion to all interspaces and also to the total motion of the specimens

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ÖSTEN HEDSTRÖM

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A CLINICAL AND EXPERIMENTAL STUDY

ACTA ORTHOPAEDICA SCANDINAVICA
SUPPLEMENTUM NR [illegible]
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ACTA ORTHOPAEDICA SCANDINAVICA

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ERRATA

Page 22 line 19 frequently occuring possibly regularly appearing phenome non provided *should read* frequently occuring possibly regularly appearing phenomenon provided
Page 35 line 10 Table 1 *should read* Table I
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Page 36 line 2 Table 2 *should read* Table II
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Page 51 line 1 cf p 00 *should read* cf p 83
Page 57 line 5 p 47 *should read* p 48
Page 57 line 9 diagram 1 and 5 *should read* Fig 12 and 14
Page 58 line 22 pp 47—48 *should read* pp 48—49
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Page 82 line 19 p 000 *should read* p 41
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ACTA ORTHOPAEDICA SCANDINAVICA
SUPPLEMENTUM No 122

From the Department of Orthopedic Surgery University Hospital Lund Sweden
(Head Professor Gunnar Wiberg)

GROWTH STIMULATION OF LONG BONES AFTER FRACTURE OR SIMILAR TRAUMA

A Clinical and Experimental Study

by

ÖSTEN HEDSTRÖM

MUNKSGAARD COPENHAGEN 1969

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INTRODUCTION

The growth of man hardly seems to have been a subject of study before the eighteenth century Up to that time it had been the object of philosophical, religious and poetical reflections Aristotle s natural philosophy considers growth to be one of the three co operating primary forces in the living organism but concrete observations of the growth of individuals do not appear to have been preserved nor probably made to judge from the loose speculations and system constructions supplied by for instance Galen So worthy a representative of natural science of the Renaissance as *Fernel* (1548) has — despite rising opposition to Aristotle — hardly anything to add to the then existing knowledge of growth

The oldest preserved systematic record of growth dates to 1759—1777 when Count *Gueneau de Montbeillard* carefully recorded every six months the increase in the height of his son A few decades earlier 1727 however the English biologist *Stephen Hales* had carried out the oldest known animal experiment on skeletal growth by boring holes in chicken bones Here he was able to show that the growth of the long bones takes place at the epiphyses and not interstitially The result was confirmed by another method by *Duhamel* (1742 1743) The surgeon *J Hunter* at the end of the eigteenth century and the physiologist *Flourens* at the mid nineteenth century carried out related investigations

Towards the end of the nineteenth century a rapidly increasing number of investigations by anatomists and physiologists into the morphology and physiology of bone tissue were made wherein the skeletal growth was given increased consideration Because the growth of the individual and the skeleton from a mathematical standpoint can be regarded as a special example of the velocity concept (length increase/time unit) two deviations from the regular norm were encountered at a closer study of it acceleration and retardation Already *Montbeillard s* growth diagram had proved that both these variants occur during a child s normal development Apart from this it has always been known that the growth process can be slowed or can stop for a variety of causes (dwarfism shortening of the extremities after polio &c) although the causal connexion has been obscure That many factors on the other hand can induce growth acceleration has seemed improbable it could only be demonstrated by more thorough scientific investigation of growing individuals

PART TWO

EXPERIMENTAL STUDY OF GROWTH REACTIONS FROM PROXIMAL AND DISTAL GROWTH REGIONS AFTER *CORTICAL DRILLING*

INTRODUCTION

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During the latter half of the nineteenth century, however, several scientists found that fracture in a long bone in a growing person could apparently *induce a growth stimulus in the broken bone* and possibly also in adjoining long bones This phenomenon was received with interest by the experimental orthopaedics, and the course of growth after both fractures and other traumata to the extremities has been studied in a large number of investigations from *Ollier* (1867) up to the present The hopes of gaining in this way a deepened insight into the nature of skeletal growth and also into the healing of fractures have in some respects been fulfilled, but in others thwarted by inaccurate measuring methods

The demonstration of this growth acceleration and its mapping by experimental methods has been of considerable practical importance for clinical orthopaedics both at the investigation into the reasons for the frequently ocurring difference in bone length and at the treatment of it The study of retarded growth has, of course, correspondingly given valuable information in the mentioned respects

A person whose arm lengths differ by a few cm is often unconscious of it as are those around him It is natural therefore that arm length differences were earlier rarely mentioned, much less reported and *Ehalt* (1958) observes *en passant "Verkurzungen bzw. Verlangerungen an der oberen Extremitat sind uninteressant"*

Wiberg and *Emneus* at the Orthopaedic Clinic in Lund started in 1955 systematic investigations of the length conditions in growing humerus after fracture This bone was chosen for the following reason

Three distinctly different types of fracture in humerus appear in children metaphyseal fractures through the surgical neck metaphyseal fractures through the supracondylar region the genuine diaphysis fracture (the epicondylar fractures are disregarded here) Comparison between the degrees of growth increase at these three types of fractures could be thought to disclose whether the localization of the fracture in relation to proximal and distal epiphyses has any relation to the extent of the growth stimulus, more briefly, whether the growth increase varies with the level of the fracture

At the 28th assembly of the Nordisk Ortopedisk Forening held in Helsinki in 1956, where growth problems were among the main themes *Emneus* submitted a first preliminary report concerning these investigations Forty instances of fractured humerus were accounted for where all three of the above mentioned types of fractures were represented and where the length of humerus was established by rontgenological measurement according to orthodiagraphic method Only one measurement was made

in each case and this had taken place 18 months to 8 years after the accident The result of the investigation was briefly that overgrowth of 3 to 20 mm could be demonstrated in 34 cases and that no relation between the degree of dislocation of the fracture and the growth acceleration could be proved Otherwise the limited material permitted no conclusions about a possible relation between fracture level and growth increase

At the SICOT congress in Barcelona in 1957 *Emneus* and *Wiberg* presented a more detailed report on the effect of fractures on the growth in humerus As with the Helsinki report two problems were posed

1 How often does an increase in growth occur after fracture in growing long bone?
2 Does a possible increment in length vary with the fracture level?

This time an attempt had been made to carry out a more detailed investigation by repeated measurements with regular time intervals This procedure also meant that the answer to a further question could be sought

3 When does the growth acceleration begin and when does it end?

The material now consisted of 49 cases and increase in length could be demonstrated in 44 of them The interval between trauma and measurement varied in this series from 18 months to 9 years

Question 2 could not be answered definitely The values of the measurements obtained were not considered to provide positive evidence of any relation between the size of the growth stimulus and the level of the fracture

To find an answer to question 3 an attempt had been made to carry out humerus measurements at three month intervals during the course of approximately 18 months beginning 2—4 months after the accident Only 5 patients had made themselves available Only one of these came to all 6 investigations The obtained diagrams of the increase in growth were therefore highly approximative The time when measurable accelerated growth began seemed to be 4 possibly 2 months after the accident With equally strong reservations for insufficient number of measurements the growth stimulus could be supposed to continue for 2 years after the trauma naturally providing that the growth plates in humerus still remained open

Emneus and *Hedstrom* published a supplementary report in 1964 The material had now increased to 70 fractures (44 supracondylar 11 diaphyseal 15 through the surgical neck) and overgrowth was measured in 63 cases Measurement series had to a large extent been attempted at regular intervals and 21 growth diagrams — considerably defective in parts —

could be presented From these the authors believed they could interpret that growth stimulation (counted from the day of the fracture) went on for 12 months in 6 cases, 18 months in 10, and even longer in 4 As in the two previous investigations, it was not possible with any degree of certainty to *determine when the growth stimulus starts,* nor *did the fracture level show* any obvious relation to the size of the increase in growth in this series

The above-mentioned three sub-reports had thus only roughly answered the posed questions It was thought reasonable however, that continued work along the given lines should make possible better statistical evaluation and result in one or more scientifically valid conclusions This continued and intensified investigation is reported in this paper The approach to the problems has been amplified somewhat Solutions of the following questions have been sought

1 Is growth stimulus after fracture in growing humerus a constant phenomenon?

2 Does this growth stimulus vary with
   a) the degree of dislocation?
   b) the distance of the fracture from the growth regions?
   c) the age of the individual?

3 How soon after fracture can growth stimulus be demonstrated and *when does it end?*

4 Does the thus developed bone length difference show signs of adjustment during the continued course of growth?

The investigation is thus primarily of a clinical character, and this aspect is reported in the following *Part One*

At a relatively early stage of the investigation it became evident that the clinical material was not sufficient to provide answers to all the problems stated above esp question 2 b Consequently experimental studies were introduced as a complement This experimental work is reported in *Part Two*

PART ONE

Growth Stimulation After Humerus Fractures in Children

CHAPTER I

EARLIER STUDIES OF ACCELERATED GROWTH IN HOMO, WITH SPECIAL REFERENCE TO FRACTURE

A Normal phenomena of importance when appraising growth stimulus

1 Physiological anisomelia

A difference in length between two equivalent contralateral long bones or extremities — anisomelia — can, of course be conspicuos as in congenital hypoplasia or aplasia, after early poliomyelitis, &c but mostly the differences found are comparatively small being only a few per cent of the total length of the bone in question If we wish to determine whether a growth stimulation is the cause of the small recorded difference in length we must know the mutual length proportions of the measurement objects at the time the stimulating factor begins to act In several clinical and experimental studies of skeletal growth however, it has been presumed that the length of equivalent long bones from the right and the left sides of the body is identical According to several scientists, this presumption is not justified On the contrary a physiological anisomelia seems to be possibly just as common as a real isomelia *Bristow* (1909) at direct measurement of femora in an obduction material found an average difference in length of 3 mm in 68 per cent *Levander* (1929) established with the aid of rontgenological measurement an average variation in femur of ± 2 mm in 6 out of 20 persons (30 %)

Rush & Steiner (1946) measured rontgenographically 1 000 soldiers chosen at random and demonstrated different leg lengths in 77 per cent with an average deviation of 7 mm *Hjort Guldhammer* (1963) examined an archaeological skeletal material of femora from 102 persons and tibiae from 78 He recorded for both kinds of long bones an anisomelia in 89 per cent where, however, in approximately 50 per cent the difference in length did not exceed 2 mm

Similar to other growth studies there has not been any great interest in

the upper extremities in this respect, and no exact values concerning physiological anisomelia in humerus have been found in the literature None the less it is reasonable to presume a certain normal mutual variation in length of this bone

Before the study of the growth disturbances in the long bones is subjected to a historical survey it must thus be concluded that full symmetry cannot be depended on between the two sides of the body, as far as the length of the skeletal parts is concerned

2 Different growth intensity in the proximal and the distal bone ends

At a more close analysis of accelerated growth it is important to take into consideration that the increase in length does not occur at an identical rate from the proximal and the distal growth regions of the long bones *Hales* (1731) and *Duhamel* (1742 1743) who investigated skeletal growth were the first to report this in the literature It has gradually become the object of more precise determinations With the aid of various kinds of indicators placer in the diaphysis and by direct or rontgenological measurement the approximate values for the percentage proportion of the growth from each epiphyseal plate have been obtained although the values diverge somewhat in different series (for homo *Digby* 1916 *Bergmann* 1928 *Gill & Abbot* 1942 *Hendryson* 1945 *Green & Anderson* 1947 *Goff* 1960 *Anderson Green & Messner* 1963) The values for humerus (total growth) are given by two of those authors

	Proximal growth plate	Distal growth plate
Digby	80	20
Bergmann	75	25

Digby used *can a nutritia* as indicator *Hendryson* found this unreliable *Bergmann* on the other hand used metaphyseal condensation lines appearing on the rontgen pictures as foundation for his measurements On the basis of these investigations the total growth proportion from the proximal end of humerus in homo thus seems to be 3—4 *times larger than* from the distal

Here it can be noted that the growth activity from the ends of the long bones does not cease at the same time which as far as humerus is concerned is shown in Fig 4 *Humphry's* observation from 1861 should also be mentioned that the epiphyseal plate with the lower growth potential is the one which becomes obliterated first

CHAPTER I

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et al (1963) Venous stasis produced by vessel ligature or by tourniquet has been tried by *inter al* *Borel* (1922) *Bergmann* (1931) *Kishikawa* (1936) *Servelle* (1948), *Hutchison & Burdeaux* (1954) *Hansson* (1969 in press)

Concerning inflammatory stimuli the growth stimulating effect of diaphyseal osteomyelitis was observed early probably first by *Stanley* (1849) later by *Paget* (1863) *Ollier* (1867) *Bergmann* (1931) and *Trueta* (1953) *M Brattstrom* (1963) established growth increase in femur and to some extent in tibia at juvenile rheumatoid gonarthritis — An effect probably related in nature was obtained at the many experiments carried out by the implantation of diverse materials foreign to the body juxta epiphysially or intramedullarly (see e g *Meisenbach* 1910 *Pitzen* 1928 *Bohlmann* 1929 *Kishikawa* 1936 *Wu & Miltner* 1937 *Chapchal & Zeldenrust* 1948 *Pease* 1952 *Nordentoft & Guldhammer* 1964) Heating of growth zones according to *Ring & Lee* (1958) causes no growth reaction whereas *Richards & Stofer* (1959) found obvious growth increase after electrical heating *Barr et al* (1943) reported no or negative effect from rontgen radiation Growth increase on the basis of neoplastic changes was recorded by *Harris* (1962) in fibrous dysplasia *McCarroll* (1950) *inter al* noted several instances of bone hypertrophy in neurofibromatosis (von Recklinghausen s disease)

The effect of fractures on skeletal growth the main theme of the present work is discussed in more detail in Section 2 (p 16) A closely related lesion the one produced when cutting out tibial grafts was shown to cause moderate growth increases in series published by *Compere & Adams* (1937) and *Breine & Johansson* (1966)

The experimental reproductions of traumatic stimuli whether artificial fractures drillings periosteal strippings or other are discussed in *Part Two* where the author describes his use of such a method of producing growth increase in long bone in rabbit

Poliomyelitis as a growth stimulating factor is in parentheses in the above table because this disease when paralysis and trophic disturbances have become fully developed regularly results in growth inhibition However a temporary acceleration of the growth is often noted (*Ollier* 1867 *Lerique* 1956 *Trott et al* 1958 *Ratliff* 1959 *Ring* 1961) in the paralysed extremity during the first year after the onset of the disease The causal connexion is not fully clear here

Many investigators have attempted in experiments to imitate the poliomyelitis lesions by cutting anterior nerve roots or peripheral nerves Conflicting results were obtained concerning growth stimulus *Ring* (1961) and *Sw den* (1967) demonstrated increased growth after the two mentioned

B Survey of the literature concerning stimulation o skeletal growth

1 Brief summary of earlier studies of bone growth stimulation in gener

The literature on accelerated growth has with time become copious extensive reviews have been given by several authors For comprehe surveys the reader is referred to *inter al Goff* (1960), *Taillard & Mor* (1965), *Hansson* (1967), *Sunden* (1967)

At a closer examination of the factors that can stimulate bone gro four main types can be distinguished These are clinically represented, are thus based on different pathological changes For study purposes, ex mental correspondences to these categories have been developed, i e var types of operations, some of which have found clinical application following table shows the clinically occurring growth accelerating sti and their experimental equivalents A fifth category — with someti stimulating, but more often inhibiting effect — has been added in pa theses

Clinically ocurring stimuli	*Experimental stimuli*
congenital	arteriovenous fistula venous stasis
inflammatory	implantation of foreign material heat rontgen
neoplastic	no correspondence
traumatic	experimental fractures, periosteal stripping trauma to bone marrow
(poliomyelitis)	different examples of lesions of peripheral nerv

Among stimuli of congenital nature ocurring clinically can be mention *Klippel-Trenaunay s* (1900) syndrome with cutaneous haemangioma va ces, and local hypertrophy Haemophilia has been reported to result increased growth of long bones on both sides of an arthropathic join usually the knee joint (*inter al Taillard & Morscher 1965*) With regard experimental equivalents vascular deformities have been reproduced b many investigators such as *Janes & Musgrove* (1950) *Hiertonn* (1957 *Doerr & Janes* (1959) *Kelly Janes & Peterson* (1959) *Vanderhoeft Kell*

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B Survey of the literature concerning stimulation of skeletal growth

1 Brief summary of earlier studies of bone growth stimulation in general

The literature on accelerated growth has with time become copious and extensive reviews have been given by several authors For comprehensive surveys the reader is referred to *inter al Goff* (1960), *Taillard & Morscher* (1965), *Hansson* (1967), *Sunden* (1967)

At a closer examination of the factors that can stimulate bone growth four main types can be distinguished These are clinically represented and are thus based on different pathological changes For study purposes, experimental correspondences to these categories have been developed, i e various types of operations, some of which have found clinical application The following table shows the clinically occurring growth accelerating stimuli and their experimental equivalents A fifth category — with sometimes stimulating, but more often inhibiting, effect — has been added in parentheses

Clinically ocurring stimuli	*Experimental stimuli*
congenital	arteriovenous fistula venous stasis
inflammatory	implantation of foreign material heat, rontgen
neoplastic	no correspondence
traumatic	experimental fractures, periosteal stripping trauma to bone marrow
(poliomyelitis)	different examples of lesions of peripheral nerves

Among stimuli of congenital nature ocurring clinically can be mentioned *Klippel-Trenaunay's* (1900) syndrome with cutaneous haemangioma, varices, and local hypertrophy Haemophilia has been reported to result in increased growth of long bones on both sides of an arthropathic joint usually the knee joint (*inter al Taillard & Morscher* 1965) With regard to experimental equivalents vascular deformities have been reproduced by many investigators such as *Janes & Musgrove* (1950) *Hiertonn* (1957) *Doerr & Janes* (1959) *Kelly Janes & Peterson* (1959) *Vanderhoeft Kelly*

of the cases had undergone osteosynthesis with Lane plate which can in itself be thought to stimulate growth

Shortly afterwards *Burdick & Siris* (1923) reported a large material of fractures of the shaft of femur in children Of these 118 had at discharge from hospital a shortening of the bone of 0 5 to 3 cm (the measuring method is not described) Within 3 years 53 of them had spontaneously attained bone length equality, and 14 others showed obvious reduction in the length difference The authors make no theoretical deliberations instead they draw the practical conclusion that a slight shortening in fractures of this nature must not necessarily be corrected

In 1923 *Speed* published an article wherein he mainly discussed over growth in relation to osteomyelitis but where in the introduction he mentioned in pa sing that he had observed about 20 cases of so called compensatory overgrowth which refers precisely to these growth accelera tions in fractured (and primarily shortened at healing) femora In 1924 *David* reported a series of 71 diaphyseal femur fractures where with the aid of repeated rontgenological measurements he could demonstrate that 62 of them completely or partly had been able to correct the reduction in the length of the fractured bone that existed at the end of the fixation treat ment

Cole (1922 1925) presented smaller series also measured rontgenologi cally and made in the main the same findings as *David* but also noted in 2 cases of fractured femur that not only femur but also tibia on the same side had increased in length *Conwell* (1929) was of the opinion that skeletal overgrowth chiefly occurred before 8 years of age *Clark* (1926) out of 31 cases of fractured femur could not find any with increase in growth

An interesting analysis was published in 1929 by *Levander* In a thesis on the treatment of shaft fractures of the femur a special chapter referred to increased growth in length of the long bones of the lower extremity after fracture As mentioned earlier (p 12) *Levander* began his investigation by determining the possible occurrence of physiological difference in length between contralateral equivalent long bones in a normal material to enable him to stand on firmer ground at a following measurement of the fracture cases The values obtained for physiological anisomelia however were negligible Determinations of bone length were then carried out by ront genological measuring technique on 48 femur fracture patients aged from 1 to 16 years of whom 46 showed positive increase in length varying from 4 to 40 mm No obvious relation between the extent of the add d length and the localization, form and treatment of the fracture could be proved nor

forms of motor denervation, whereas *Gillespie* (1954) *Troupp* (1961), *inter al*, observed growth inhibition Lumbar sympathectomies have often resulted in insignificant or no overgrowth (*Cannon et al* 1929, *Bisgard* 1933, *Kishikawa* 1936, *Harris & McDonald* 1936 *Ring* 1961)

This section has thus, in a brief survey, dealt with forms of natural and artificial growth acceleration that are not immediately related to the present author's own investigations

2 *Earlier investigations of the growth stimulating effect of fractures*

Most investigations published in Anglo Saxon, French German and Scandinavian literature which treat overgrowth after fracture refer to femur, whereas few deal with tibia, radius, and ulna Humerus has not been the object of any special study, except for the earlier mentioned investigations by *Emneus* (1956) *Emneus & Wiberg* (1957), and *Emneus & Hedström* (1964) Brief references are made in passing to humeral overgrowth by *Budig* (1957), *Razanelli & Prinstl* (1958) and *Murayama* (1963) A larger investigation of more fundamental nature into growth acceleration, in which humerus was also examined was published in 1959 by *Calati & Poli* and is referred to in more detail on p 21

There is no reason for supposing that essential differences could exist concerning the growth conditions for various kinds of long bones When a survey of the studies in this field — mainly concentrated to femur — is now presented the intention is that facts and hypotheses extracted therefrom should then form a discussion basis for the present author's analysis of the post-traumatic growth stimulus in humerus

Ollier is often described as the discoverer of the growth increase after fracture of growing long bones However the phenomenon has been known earlier it was mentioned by *Volkmann (1862)* From *Ollier's* much varied and well documented studies from 1867, we learn that fracture in growing femur or tibia can result in at least 1 cm increase in length *v Langenbeck* in 1869 observed that increased longitudinal growth can occur after contusion of the diaphysis regions During the next decades, similar individual reports appeared (e g *Carlsson* 1918), usually as marginal notes to records of treatment and treatment results in femur fractures

Truesdell (1921) was the first to use the post traumatic increase in growth as a theme for an article Without describing his measuring technique he presented 5 cases of femoral shaft fracture with on average 2 5 cm increase in length The observation does not permit any conclusions especially as 2

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any relation to the age of the patient The duration of the growth acceleration was estimated at 2 to 3 years Of the patients, 8 were also investigated concerning possible increase in length of tibia in the fractured extremity growth increase of 3 to 7 mm was established in 5 patients

Contrary to *Speed*, *Cole*, and others, who regarded increase in growth after fracture as compensatory and possibly *conditioned by mechanical causes* *Levander* believed that the increase in growth was triggered off by *post traumatic hyperaemia in and around the fractured bone*, and seems to have been the first to propound this theory It is true that *Lexer* in 1922 was able to demonstrate a marked and long lasting increase in the vascularity around fractures, but he did not associate this with the phenomenon of overgrowth In the same investigation Levander tried to support his hypothesis by the use of experimental studies (these are reported in Part Two) In his summary, *Levander* concluded that growth stimulus after fracture of growing long bone was a constant phenomenon and that its duration was 2—3 years moreover, fracture of a long bone under certain, unknown conditions could *also result in an increase in growth in other long bones in the same* extremity

Ferguson (1933), finding that after tibia osteotomy in children a relative reduction in the fibula of the same side could be noted realized that this *must be due to accelerated growth of the operated tibia and developed on* the basis of this observation a theory that the increase in growth must be conditioned by the interrupted *blood supply from the medullary vessels to* the metaphysis and by redirection resulting from this of blood to the still intact periosteal and epiphyseal vessels The same line of reasoning could apply to the growth stimulus in diaphyseal fractures On the basis of this he developed an operation method for producing bone elongation drilling of the cortex and curettage of the medulla via the drilled hole Increases of growth of 2—3 mm could be recorded

The works of *Ferguson* and *Levander* as well as experimental studies by *Bisgard* (1936) *Kishikawa* (1936) *Wu & Miltner* (1937) and *Compere & Adams* (1937) resulted in the vague theory of compensatory increase in growth being abandoned Instead the circulation disturbance and the *periosteal injury produced by* the trauma began to be held mainly responsible for overgrowth after fracture

Aitken in 1940 *published* a follow-up investigation of 65 femur fractures in children Of these 8 had been operated on all showed marked increase in growth *whereas of the remaining 57* treated conservatively 55 showed added length of varying degree A fairly detailed article about growth increase was *published by Blomqvist & Rudstrom* in 1943 An analysis was

made of 50 cases all femur fractures Regarding age the largest average growth stimulus occurred in the age groups 2—4 years and 6—10 years The increase in length in these ages averaged 12 mm (rontgenological measuring method) Only 7 cases showed no or uncertain overgrowth The growth acceleration which in many instances was demonstrable up to 2 years after the accident, was usually most pronounced during the first year The material included 11 operated patients and those of them who had undergone osteosynthesis showed high values of overgrowth The authors also used these osteosynthesis cases as a control of *Bergmann s* (cf p 13) determination of the different growth proportions from proximal and distal cartilage plates and obtained similar results *Hedberg* (1944) examined a material of 44 femur fractures in children and found growth increase in 38 of them with an average value of 9 mm Increase above the average value was found in the ages 4—8 years

During the past two decades several articles have appeared wherein fundamentally similar results have been published (see for instance *Oeconomos* 1948 *Lorthioir & Soeur* 1948 *Potts & Dunham* 1949 *Schuttemeyer & Flach* 1950 *Odell & Leydig* 1951 *Greville & Ivins* 1957 *Neer & Cadman* 1957 *Pease* 1957 *Schenk* 1957 *Ingelrans Lacheretz & Poupard* 1958 *Calati & Poli* 1959 *Neves* 1959 *Krebs & Streicher* 1960 *Singer & Kraft* 1961 *Vontobel Genton & Schmid* 1961 *Flach & Kudlich* 1962 *Henry* 1963 *Weber* 1963 *Miyagi & Murayama* 1964 *Greve & Niemann* 1966 *Flach Geisbe & Fendel* 1967)

A systematic survey of all these articles however would take up too much space apart from adding nothing essentially new to the discussion but for the sake of greater surveyability a summary of the gained results is given at the end of this section None the less there is reason to refer specially to W P *Blount s* activity within bone growth research Although this particularly aims at the treatment of bone length difference he has in several articles (1944 1950 1952 1960) and not least in his monography Fractures in Children (1954) disseminated knowledge of the increased growth after fractures in growing bone and has suggested how this can be prevented from reaching dimensions disturbing to the static conditions of the individual According to *Blount* open repositions of diaphyseal fractures are practically never indicated they are associated with the risk of especially strong increase in growth Repeated correcting manipulations during the course of healing have the same damaging effect Although *Blount* finds the size of the growth increase difficult to appraise beforehand he recommends that the diaphyseal femur fractures in children be allowed to heal with a reduction of 1—2 *cm* which will highly probably be

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A very extensive literature treats humerus fractures in children particularly supracondylar fractures but the interest is as a rule directed on therapeutic problems and as already indicated there is usually no information about stimulus of the longitudinal growth of humerus The author could trace only 3 works that discussed this phenomenon

In 1957 *Budig* reported the final results of a great many instances of epiphyseolysis and fracture close to or involving the proximal growth plate of humerus Regarding the former he established as expected a number of growth reductions because of the epiphyseal lesion When *Budig* similarly measured the pure fracture cases which thus showed fracture through the surgical neck he found out of 50 patients 7 with elongation of the humerus amounting to up to 3 cm A number of reduction were also recorded in the same group probably due to the fractures having engaged the growth region without this appearing in the rontgen pictures

In a follow up study of supracondylar humerus fractures from 1958 *Ravanelli & Prinstl* observed an increase in width metaphysially in 46 % of the patients Length measurement however was not made

Calati & Poli in 1959 presented a material of 165 rontgenologically measured diaphysis fractures from femur tibia humerus radius/ulna and clavicle They found different frequencies for growth increase in these bones for femur and tibia 63 6 % and 60 % respectively for humerus 27 7 % and for clavicle zero At the same time they admitted that the percentage can be higher because fractures that heal with considerable shortening can be thought to trigger of an overgrowth although not large enough for the fractured bone to become equally as long as or longer than the bone on the healthy side The absolute size of overgrowth was found to be larger for femur and tibia than for the long bones of the arms The authors considered that elongation resulting from growth stimulus is probably permanent that metaphyseal fractures produce slighter increase in growth than do diaphyseal fractures and that the added length is possibly proportional to the dislocation of the fracture and the extent of periosteal lesion Concerning the genesis of the changed growth rate the authors discuss *Trueta's* theory about the destruction of the *nutritional* circulation and the increased blood supply to the growth region This theory is set against the hypothesis of *Lacroix concerning* a specific agent that stimulates bone formation osteogenin which could be released in the fracture and which possibly could not only have an effect on the fractured bone but also perhaps exert some remote effect on the skeleton as a whole Some

eliminated during the course of further growth The same author cannot demonstrate any relation between the distance of the fracture from the growth plates and the size of the overgrowth, he finds no tendency for spontaneous recovery of the difference in length arising from growth stimulus

Two works of Danish authors are worthy of a more detailed examination Both are specially devoted to the growth stimulus after fracture *Barfod & Christensen* in 1958 published a follow-up study of 114 femur fractures, wherein, however, they restricted themselves to the use of a tape measure as measuring method, this obviously limits the value of the investigation Contrary to most earlier investigators they separated conservatively treated from operatively treated At a follow-up study, both categories showed overgrowth, although this was considerably more pronounced in the operated cases The growth stimulus was judged to last for about 2 years Oblique and comminute fractures were shown to produce more overgrowth than transverse fractures, whereas there was insufficient material to enable them to decide the possible importance of the position of the fracture in relation to the growth regions No positive sex difference could be demonstrated whereas concerning the effect of age, it was possible to record that children less than 3 years of age showed slightly weaker increase in growth after trauma than did the age group 3—15 years, where the growth acceleration appeared both more rapid as well as fairly homogeneous Elongation of the tibia of the same side, in femur diaphysis fracture occurred in 6 out of 93 cases, with values lying between 5 and 10 mm

In 1963, *Hjort Guldhammer* presented a thesis devoted to growth stimulus after fracture in the lower extremity in children The investigation was based on orthodiagraphic length determinations mostly single measurements made at different time intervals after the trauma but also series of repeated measurements Compared with investigations referred to earlier much information is obtained concerning the effect of tibia fractures on growth Fairly regularly *Hjort Guldhammer* found increase in growth in tibia after dislocated transverse or oblique fracture averaging 8 mm At non dislocated fracture on the other hand the bone length increases on average 3 mm The growth acceleration is said to start immediately after the trauma and stops within the course of 18 to 24 months The average overgrowth for femur is determined at 13 mm for dislocated fractures but at zero for infraction Children aged 0—4 years have a growth increase averaging 11 mm children more than 4 years 14 mm No ipsilateral growth stimulus can be proved in femur at tibia fracture Obversely, no ipsilateral growth stimulus can be proved in tibia at femur fracture

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support for the existence of such a factor is given by the authors in their observations of so called growth arrest striae (*Harris* 1933, *Trueta* 1953) not only in the metaphysis of the damaged long bone but also in other long bones in other extremities

Miyagi and *Murayama* in their study from 1964 have also measured repeatedly about a hundred diaphyseal fractures among them 6 humeri Overgrowth in this series is common, but not inevitable It is most pronounced between 3 and 10 years of age, seems to continue for about 3 years and results in permanent elongation The increase in length in the humerus has in no case exceeded 10 mm

With the object of getting greater surveyability, it seems desirable here to list present known facts and accepted hypotheses concerning growth stimulus after fracture of growing long bone such as could be derived from monographs and large summary articles by *Goff* 1960, *Flach & Kudlich* 1962, *Taillard & Morscher* 1965, *Flach Geisbe & Fendel* 1967

It can be gathered from the literature

that growth stimulus after fracture *does* occur in the long bones of both the lower and the upper extremities

that this growth increase is a frequently occurring possibly regularly appearing phenomenon, provided the fracture is dislocated

that dislocated and/or comminuted fractures are probably accompanied by particularly marked growth stimulus

that children during the first 2—4 years of their life might show comparatively slight growth acceleration

that growth stimulus most often becomes noticeable fairly early in the course of healing probably 2—3 months after the accident

and that it continues as long as reconstruction processes and increased blood circulation occur in the injured bone i e *circa* 2 years

that an established length difference is not to any appreciable extent eliminated by some later form of change in growth

However, it is not positively stated in the literature

whether the fracture level in the long bone has any significance for the size of the increase in growth

whether adjoining long bones show to a greater or lesser extent the same increase in growth as the fractured bone

If the problems posed by the present author are set in relation to the investigation results taken from the literature it would seem that the answers to the various questions on p 10 can in no case be regarded as guaranteed No correlation between fracture level and growth stimulus has been proved and the relation of the increase in growth to the age of the individual as well as its development in time cannot be considered known with any particular degree of accuracy

CHAPTER II

MATERIAL

The material consists of humerus fractures Because certain clinical and anatomical designations or phenomena concerning humerus could call for some comment or definition, it was thought fitting to give a brief introductory description of humerus and of the fracture types discussed in this work Beside this, it was also judged necessary to define some general concepts about long bones, because the nomenclature varies with different authors The account is restricted to those phenomena directly related to the *objective and the completion of the investigation*

A Some anatomical terms

The terminology *used here concerning the main parts of a growing long* bone agrees with that used by *Hansson* (1967) in his thesis on longitudinal bone growth in rabbits Thus according to Fig 1 there is a distinction between a diaphysis and the two end regions Reckoned from the middle the diaphysis is composed of the shaft proper and the metaphyses which border on the end regions In central direction the metaphysis extends as far as the bone substance *is spongy in texture The epiphysis contains a* central bone nucleus (in places several) the bony epiphysis surrounded by a cartilaginous shell the growth cartilage of the epiphysis Between the diaphysis and the bony epiphysis there is a cartilaginous zone from now on called the growth plate which from a physiological standpoint can be considered as consisting of two layers one terminal belonging to the epiphysis — *the growth cartilage of epiphysis — and one central bordering* on the diaphysis — the growth cartilage of diaphysis In the former the

growth occurs distally reckoned from the middle of the bone in the latter centrally The firstmentioned centrifugal growth is on a small scale and probably ceases altogether early in the life of the individual

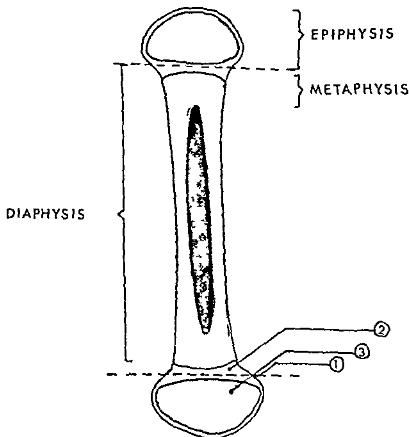


Fig 1 Principal parts of a long bone

1 growth cartilage of the epiphysis
2 growth plate of the diaphysis } *the cartilage plate*
3 bony epiphysis

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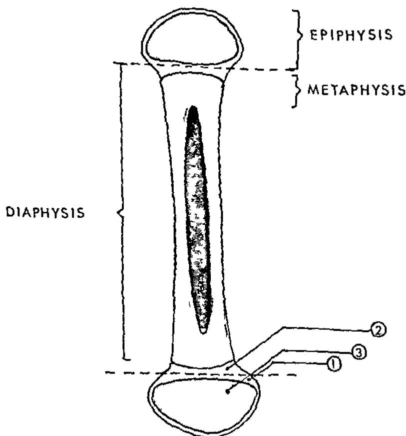


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2 g ou th plate of the diaphysis
3 bony epiphysis

B *Some anatomical observations concerning humerus*

The almost hemispherical, cartilage covered *caput humeri* is distally delimited by a narrow ring-formed groove, *collum anatomicum*. The cranial part of this groove forms the border between the humeral head and the two

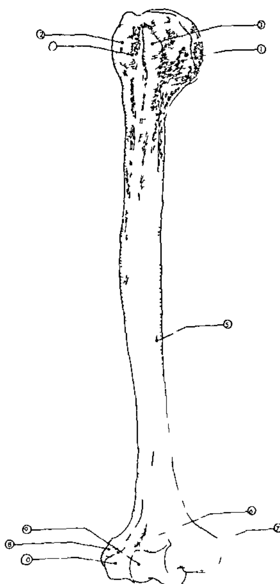


Fig 2 Front of right humerus

1 collum anatomicum
2 tuberculum majus
3 tuberculum minus
4 the bicipital groove
5 nutrient foramen of the diaphysis
6 coronoid fossa
7 medial epicondyle
8 lateral epicondyle
9 trochlea
10 capitulum humeri

tuberosities. The greater tuberosity is the large prominence at the upper end of the lateral surface of the humerus. There is no clear distal border to this tuberosity. It slopes in a slight arc down towards the diaphysis.

The minor tuberosity which is separated from the other by the bicipital groove faces directly forwards and its distal border is somewhat more distinct than in the case of the greater tuberosity

Immediately distal to these two tuberosities lies the surgical neck This section is often not clearly defined concerning its distal delimitation However the author chooses to define the extent of the surgical neck in accordance with *Anson & Maddock* (1933 from the lower limit of the tuberosities to the insertion of the axillary muscles into the intertubercular sulcus Unfortunately this limit cannot be distinguished on rontgen pictures of humerus the rontgenological indication of the surgical neck is therefore somewhat optional but no better demarcation line can be proposed

Regarding the proximally cylindrical distally three sided prismatic diaphysis only the position of the nutrient foramen will be dealt with here *Carroll* (1963) has made a study of the position of this orifice in homo and found that in most instances it is situated within a small area on the medial aspect of the distal half of the middle third of the shaft Other diaphyseal nutrient foramina macroscopically visible were rare in *Carroll* s material he therefore concludes that the predominant part of the blood supply of the diaphysis and the medulla occurs via the first mentioned, usually medially situated orifice

The border between the diaphysis and the distal metaphysis (the supra condylar zone) in humerus is difficult to establish at external inspection To count with finger breadths from the joint surface as suggested in some anatomical textbooks is not suitable when referring to a material of growing individuals with big variations in the length of humerus To indicate the uppermost attachment point for the forearm musculature as upper limit (i e the insertion for m brachioradialis) would mean that a considerable part of what from a clinical standpoint is regarded as diaphysis would be included in the supracondylar region Instead the author chooses as limit a plane lying at right angles to the longitudinal axis of humerus and passing through the most cranial point of fossa olecrani This plane can without difficulty be established on the rontgen picture Regarding the region of the supracondylar humerus fractures however see p 31

The shape of the distal end of the humerus is characterized by the divergence between the radial and ulnar margins already begun in the diaphysis These margins furthest distally form the lateral and the medial epicondyle between which the deep olecranon fossa lies on the dorsal side and the coronoid fossa on the volar side In the distal joint surface of humerus there is a radial protrusion with a spherical contour when viewed

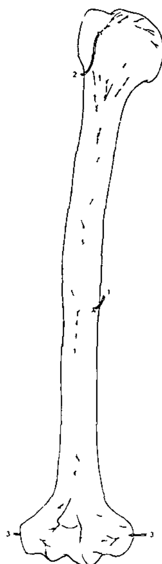


Fig 3 The main sources of the arterial supply of the humerus

1 main nutrient artery of the diaphysis
2 anterolateral branch of the anterior humeral circumflex artery
3 smaller nutrient arteries of the epicondyles

from the volar side *capitulum humeri* In an ulnar direction from this and separated from it by a groove lies the hour-glass shaped *trochlea humeri*

Laing (1956) has studied the distribution of the arterial vessels in adult humerus According to him the proximal end of the humerus is richly supplied by branches from a nutrient artery which in its turn issues from the anterior humeral circumflex artery The nutrient artery which penetrates into the diaphysis via the nutrient foramen could be shown to have

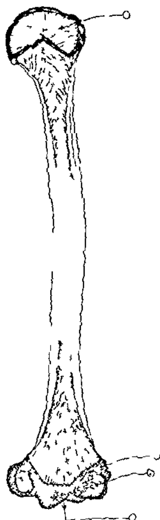


Fig. 4 Ossification centres of the humerus at an approx. age of 13 years (schematically after MESCHAN)

		appears at	fuse together	fuse to shaft
1 cap. humeri	caput propr.	0—3 m	4—6 yrs	18—21 yrs
	greater tub.	3—24 m		
	lesser tub.	3—5 yrs		
2 capitulum humeri		4—12 m	at puberty	14—17 yrs
3 trochlea		7—10 yrs		
4 lat. epicondyle		11—14 yrs		

two branches, one larger, ascending towards caput humeri, and one smaller descending with numerous ramifications towards the epicondyles These in turn receive arteries from outside, which are especially ramified in trochlea and capitulum The blood supply appears plentiful also in the distal end of the humerus

Quite strongly varied information concerning times for the appearance and development of ossification centres in the humerus epiphyses is given by different authors (*Paterson* 1929, *Francis & Werle* 1939, *Flecker* 1942, *Elgenmark* 1946, *Caffey* 1956, *Haraldsson* 1957, &c), which probably reflects to some extent the considerable individual differences that exis concerning skeletal development In the present work, only cases with distinct, well developed bone nuclei were meant to be used thus ossification data in Fig 4 have been exceeded by a broad margin Because the bone nucleus in *capitulum humeri* was judged to be insufficiently developed for measuring purposes in individuals aged less than 18 months they have not been included in the material

C Types of fractures and degrees of dislocation

As pointed out in the introduction this work deals with the growth stimulus in three different types of fractures

1 Fractures through the supracondylar zone
2 Fractures through the humerus diaphysis
3 Fractures through the surgical neck

The region of each of the categories is given schematically in Fig 5 Regarding the supracondylar fractures it was felt justified to abandon to some extent the upper limit of the supracondylar zone — given on p 27 — because it would otherwise have been necessary to regard as diaphyseal several V shaped fractures which have always been clinically interpreted as supracondylar Here every fracture that completely or partly occurs distally of the plane visualized through the uppermost point of *fossa olecrani* is regarded as a supracondylar fracture

Even more important in this context however is the terminal delimitation of the two fracture zones in the ends of humerus It is well known that fractures that engage a cartilage plate result for the most part in slowing or stopping the growth from this region Such a phenomenon is likely to render the judgement of possible growth acceleration more difficult consequently all such case have been eliminated from the material where on rontgen pictures fractures reach or cross over the cartilage plate or where some degree of epiphysiolysis exists

Bearing in mind how relatively close to the growth plate several fractures included here run their course it must be admitted that some slight degree of engagement of the plate itself cannot in some individual instances be altogether excluded Whether a trauma sufficiently strong to result in metaphyseal fracture is also able to cause a slight perhaps microscopic lysis of the adjacent growth plate is not known although clinical experience gives no cause for such a supposition It is most likely the forces that act in the longitudinal direction of the bone that can have a deleterious effect on the growth cartilage (Hueter Volkmann s law cf also *Blount* 1954 *Goff* 1960 *Arkin & Katz* 1965) whereas here we have mainly to deal with forces that diverge from the longitudinal axis of the humerus

Fractures are often classified with reference to the degree of dislocation or angle position to their genesis mechanism &c After attempts at distribu

two branches, one larger, ascending towards caput humeri, and one smaller descending with numerous ramifications towards the epicondyles These in turn receive arteries from outside, which are especially ramified in trochlea and capitulum The blood supply appears plentiful also in the distal end of the humerus

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This division according to dislocation has been carried out in all three investigated types of fractures It is coarse and schematic Thus the rotation factor could not be included in the calculation this is explained by the primary pictures taken of a humerus fracture not usually allowing more than an approximate estimate of rotatory faulty position Supracondylar fractures and collum chirurgicum fractures of the category + however show no signs of appreciable rotation, and concerning the diaphysary fractures in the author s material the only instance of dislocation grade + was rather a fissure without rotatory element

In the present relatively limited material a division into more than two subgroups would invalidate the statistical analysis which is why an originally planned distribution into three dislocation grades was abandoned

3

tion into three different grades according to dislocation, the author, for this investigation, has chosen to distinguish only two categories + and ++

Dislocation grade + means no or insignificant faulty position, with a *dislocation ad latus* less than 1/4 bone width, *ad axin* less than 15°

Dislocation grade ++ means that any faulty position, in one plane or more is greater than in grade + Here, is thus also included over-riding position, comminuted fractures, &c

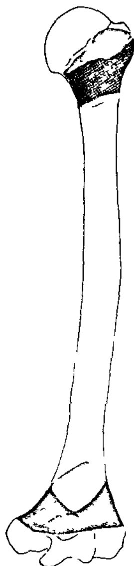


Fig 5 Extra epiphyseal fracture zones in humerus (dorsal aspect)
1 the surgical neck
2 diaphysis
3 the supracondylar region

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D Report of the fracture cases

The patient material used in the present investigation consists of 86 cases This figure has been reached as follows

During the period 1955—1966, a total of 305 cases of extra epiphyseal humerus fractures in children was registered at the Orthopaedic Clinic in Lund for follow-up measurement investigation At this primary selection all instances of multiple fractures, abdominal injuries, complicating diseases, &c were eliminated In the main only such cases were included in the present investigation where humerus fracture was the only diagnosis However, some cases with simultaneous, slight *commotio cerebri* were also included

Of the above mentioned 305 patients, 204 were rontgenologically measured on one or more occasions The first measurement was often taken in connexion with the termination of the fracture treatment and did not meet with any particular opposition from the parents it was most probably interpreted as a stage in normal follow-up of the case in question However when systematic repeated rontgen measurements (for further details, see Chapter III) were requested, the co operation of patients and relatives was considerably more difficult to obtain This is probably a common experience (cf *Oeconomos* 1948, *Chigot* 1958) concerning follow up examinations of fractures in children The reason is of course, mainly that these accident cases are so often restored to full function and that follow up examination is therefore thought by the parents to be unnecessary

From this, it might be concluded that the patients who despite the inconveniences, appear for repeated follow-up examinations also represent the most serious injuries and the most pronounced subsequent disorders However, from the following report it can be seen that the number of fractures of the lower dislocation grade is about equal to the number of more serious dislocated fractures which ought to permit an adequate comprehensive appraisal without appreciable error It must be mentioned that excessive *sequelae* on the whole do not occur in this material Operated cases were not included

As stated 204 patients underwent rontgenological measurement Of these however, no fewer than 101 failed to appear for the second measurement, thus they were excluded from this investigation Of the remaining 103 17 took part in only two measurements this cannot be considered

Ag	S p acondyla		D physe l		Coll ch		Total	
	♂	♀	♂	♀	♂	♀	♂	♀
<3y s	3	0	0	0	0	0	3	0
3 – 5	13	7	0	0	0	1	13	8
6 – 8	15	8	2	3	2	3	19	14
9 – 11	6	7	1	0	3	3	10	10
>11	1	0	1	1	5	1	7	2
	38	22	4	4	10	8	52	34
T tal	60		8		18		86	

Table I Distribution of the clinical material according to age sex and type of fracture

acceptable either However 6 of the 17 were included These had the second measurement several years later when the growth stimulus had probably ceased (i e after the onset of puberty) Although the course of growth in these patients cannot be followed in detail there are none the less initial and end values for the humerus lengths

There remains 92 patients 6 of whom were measured twice and the other 86 several times From these 86 6 were excluded (1 fracture through the growth plate 1 fracture through bone cyst and 4 technically faulty rontgen pictures) Thus 86 humerus fractures are left for the continued discussion Table 1 shows the distribution of the material on age, sex and fracture As completion it can be mentioned that the youngest patient was 20 months at the time of accident the oldest was 13 years 10 months

Although epidemiological analysis of the fracture material does not come within the scope of this work some comments of this nature can be made Table 1 gives the impression that supracondylar fractures on the average more often affect younger children than fractures through diaphysis and surgical neck If the mean age is calculated for on one hand instances of supracondylar fracture and on the other the two other categories combined 6 6 years and 9 8 years respectively are obtained a difference with high significance (observed value of statistic u=5 43***) No obvious sex differences appear A first impression from the table that girls are affected by fracture at a later age than boys does not prove valid at statistical

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CHAPTER III

METHODS

A Recording of bone lenght and longitudinal growth

The earliest growth determinations were made with tape measure and measuring rod which are still largely in use clinically where no higher demands of exactness than ±5 mm are to be met But when growth studies and treatment of bone length differences advanced a need for more accurate measuring methods arose It was then natural to try to devise a radiological technique for exact reproduction in natural size of the skeletal parts of the extremities

The earliest developed method — telerontgenography according to *Hickey* (1923) — attempted to minimize the deformation of the ends of the bone conditioned by oblique rays by maintaining the distance between rontgen tube and film as large as 7 feet or more However this proved to be impracticable and also not sufficiently exact *Bertrand & Trillat* (1948) thus reckoned with an error of 7—8 mm at such femur measuring and this despite a tube distance of 5 metres

In 1937 *Millwee* described a technique called slit scanography which employed parallel rontgen rays perpendicular to patient and film and produced with the aid of a lead filter furnished with a transverse slit A curtain of rays falling at right angles to the film was then obtained This curtain was operated by a motor alongside the object during the exposure By this procedure terminal magnification and deformation was excluded but at the cost of a fairly complicated apparatus

The orthodiagraphic method for skeletal measurements developed and modified in various ways by *Green Wyatt & Anderson* (1946) *Goldstein & Dreisinger* (1950) *Bell & Thompson* (1950) *Farril* (1953) *Taillard* (1956) *Goff* (1960) and others has resulted in simplification of the procedure so that special apparatus is no longer required and the reproduction does not suffer any angle magnification any more than it does at scanography

examination A distribution of the fracture material according to dislocation grade (Table 2) might be less interesting from a clinical standpoint, but is given because it is an important part of the later discussion (Chapter IV) and then a reference table should prove valuable

	Supracondylar				Diaphyseal				Collum chir			
	+		+ +		+		+ +		+		+ +	
	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀
Age												
< 3 yrs	2	–	1	–	–	–	–	–	–	–	–	–
3 – 5	5	3	8	4	–	–	–	–	–	–	–	1
6 – 8	6	5	9	3	1	–	1	3	–	2	2	1
9 – 11	3	3	3	4	–	–	1	–	2	1	1	2
> 11	–	–	1	–	–	–	1	1	2	–	3	1
Total	27		33		1		7		7		11	

Table II Distribution of the clinical material according to degree of fracture displacement

The treatment of the fractures will not be analysed in detail However, an examination of category dislocation + all fracture types shows that all these patients were treated solely by fixation (plaster of paris hanging cast abduction splint) without any reposition or traction whatever Contrary to this all supracondylar fractures of grade + + have undergone reposition, in 4 patients repeatedly The fractures through diaphysis and collum chirurgicum of grade + + are indicated as manually reset in 4 instances, whereas others were successively corrected during treatment with hanging cast abduction splint or wire traction With some simplification it can thus be said that the fractures of dislocation grade + were all left *in situ*, whereas the fractures of grade + + were all subjected to reposition in some form

If the error is small the measuring value can be corrected and then the calculation is based on the deviation of the central beam from the proper measuring point and the distance focus/film and object/film

The distance focus/film was 100 cm during the present investigation If the distance object/film is estimated at for instance 5 cm, the degree of magnification is approximately 1 20 (cf Fig 7) If the measuring point lies 2 cm from the central beam the error is thus 1 mm for which correction is required

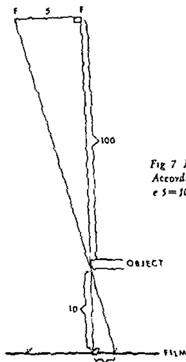


Fig 7 Measurement error at orthodiagraphy
According to the principle for equiangular triangles
e 5 = 10 100 e = 0 5
F = focus in correct position
F_1 = focus inadvertently moved 5 cm
e = measuring error

The largest error factor is probably the conscious or unconscious move ments that the patient makes during the course of photographing An insignificant movement of the shoulder easily escapes the notice of the investigator at the moment of exposure but gives considerable misrepresen tation on the film Possibly a variation in breathing phase can also result in some mm displacement of humerus particularly in children with scant development of the diaphragmatic breathing To reduce the risk of these sources of errors shoulder and wris were steadied with sandbags but smaller position adjustments can sometimes have occurred without having

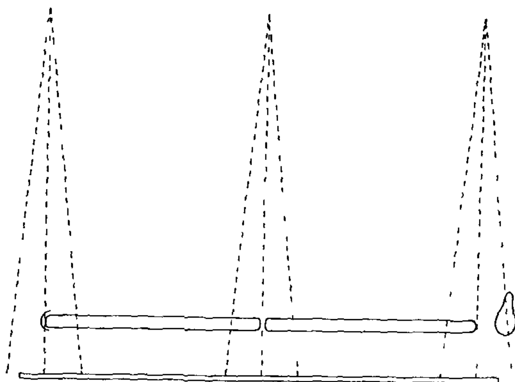


Fig 6 Diagrammatical sketch for orthodiagraphical measurement (according to Buchner Radiometrie)

Strongly collimated perpendicular beams are used As at all geometrical rontgen measurements, accurate adjustment of the patient is essential The investigated body part must be parallel with the film which in the case of the humerus means that the distal end must be raised An estimate of the object/film distance must be made in each individual instance On one and the same film separate exposures are made, at humerus investigations two at measurement of leg length three (cf Fig 6) First the tube is centred on one end of the long bone in question, thereafter it is moved to the other end of the bone for a new exposure

If the central beam goes through the measuring point the error of method can be estimated at 1 mm It is thus necessary to know the position of this vertical central beam At correctly adjusted rontgen tube the beam passes the film at a point in the centre between the reproduced collimator edges Very often an edge falls outside the film If this is judged to occur an extra exposure with very narrow clearance is made with the tube in the same position as mentioned above (*Norman* 1955)

If the central beam is aimed incorrectly i e away from the vertex of the joint surface of the bone to be measured the investigation must be redone

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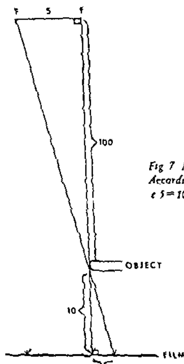


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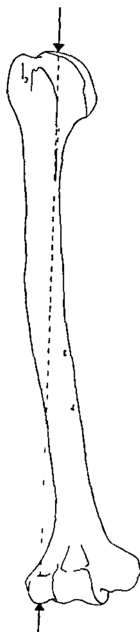


Fig 8 Determination of humeral length — distance measured

been noticed which could in turn explain isolated and obviously faulty measuring values where a humerus suddenly shows a reduction in length compared with previous investigation A change in rotation position of the upper arm results in a varied projection of *capitulum humeri* whose height can accordingly appear somewhat different This factor was taken into consideration at the investigation and the patients were instructed to rest the backs of their hands on the table

With the described technique the object is reproduced in natural size and

the sought humerus length can consequently be obtained by measuring directly on the film A more detailed description of this measuring procedure is necessary (see Fig 8)

The most distal point in the bone nucleus in *capitulum humeri* (or where ossification has ended the corresponding point on the articular surface of *capitulum*) is selected as basis From there the longest rectilinear distance is determined in humerus where the proximal end point is found to be situated on the cranial surface of the bone nucleus in *caput humeri* The distance thus measured on the rontgen picture represents the maximum length of humerus reduced by the height of the articular cartilages at the ends of the bone In case the bone nuclei needed for measuring should in some instances be different in size from their contralateral equivalents (in resemblance to the condition at congenital hip joint luxation) this could result in a certain slight rontgenological anisomelia A possible such phenomenon is not recorded however and if it exists it is eliminated by the repetition of the measurements (cf p 42) and by the primary value of the first measurement being used as basis for bone length difference and the following variations then being compared

The growth measured by this method is the total of metaphyseal and epiphyseal growth in both growth plates of humerus The epiphyseal growth however is exceedingly small compared with the metaphyseal (*Hansson* 1967) This remark is motivated by the measuring method used in the experimental part of the work where exclusively metaphyseal growth is recorded (Chapter VIII)

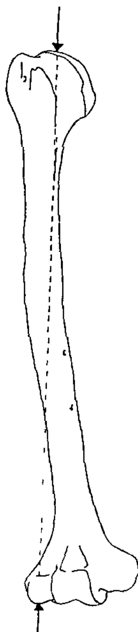


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With the described technique the object is reproduced in natural size and

No patients	No measurements
6	2
24	3
15	4
8	5
9	6
6	7
5	8
3	9
6	10
3	11
1	12
—	
86	

All patients were investigated with the same method The orthodiagraphic pictures were taken by rontgen technicians supervised by the physician responsible for the investigation who ensured that the rontgen tube was correctly adjusted and who examined the pictures obtained In conjunction with this a clinical examination was made of each proband to check the range of movement in the shoulder joint and the elbow as well as possible faulty positions On one occasion a moderate *cubitus varus* was observed which aroused suspicion of lesion of the growth plate Close examination of the primary rontgen pictures of the patient confirmed this supposition he was therefore excluded from the material Otherwise 9 cases of slight extension and flexion defects were noted however in no case of more than 15 One proband with slight Volkmann s contracture had been included in the primary material but was omitted after the first measurement 78 probands had completely normal function in the injured arm no deformity — naturally apart from length discrepancies of varying degree — and no subjective complaints

Because it would be of importance to find out whether the normally different growth rate from proximal and distal growth plate showed the same or changed proportions after fracture the insertion of a metal *indicator in* the humerus diaphysis was contemplated With the aid of this it might be possible to measure the added growth from both directions directly on the rontgen picture *Blount & Kritter* in 1959 had constructed an

B Details of the investigation

According to the original plan made in 1956 for these growth studies (see *Emnéus* 1956, *Emneus & Wiberg* 1957) the object was to make rontgenological measurements with the time schedule 3—6—9—12—15—18—21—24—30—36 months counted from the time of accident Thus 10 measurements should be made in each patient, and deviations from the schedule of more than ± 1 week should be avoided In principle this pattern was maintained during the investigation, although it became evident from the beginning that for several trivial reasons, already mentioned, both large deviations and mainly important restrictions in the measurement programme had to be accepted (see p 43)

It was also found desirable to make the first measurement considerably earlier than 3 months after the accident if possible as early as one month after the fracture fixation had been removed and the patient had regained enough mobility in his elbow to make rontgenological determination of length possible (i e an extension defect of at most 30°) With such an early examination it was hoped that it would be possible to record the humerus length before the growth stimulus had had time to give measurable effect

To gain information about the final length relations between fractured and uninjured upper arm about 30 patients whose humerus fractures had occurred 6—7 years before and had now finished growing were recalled at the end-phase of the investigation and measured in the same way

With these additions the ideal measuring schedule appeared as follows 1 (2)—3—6—9—12—15—18—21—24—30—36—72 (84) None of the patients fulfilled completely these demands and only few even approached it (because of reasons mentioned earlier) A table of the distribution of the probands on different numbers of measuring occasions shows that essentially lower investigation frequency than planned had to be accepted

No patients	No measurement
6	2
24	3
15	4
8	5
9	6
6	7
5	8
3	9
6	10
3	11
1	12
86	

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instrument for percutaneous insertion of small stainless steel markers and by courtesy of *Blount* it was possible to test a modification of this It took the form of an 8 cm lon steel pin of 1 mm calibre with a sharp point at one end and a slight indentation encircling it 5 mm above the point Under the narcosis used for resetting the humerus fracture in question the point should be driven in percutaneously in the middle of the diaphysis whereafter a slight bend would break the pin at the indentation The point would then remain steady in the diaphysis as a permanent indicator and there would probably be no need to remove it Several tests were made with this instrument but it was found that the point usually became bent and broke off before becoming sufficiently embedded in the cortex of the bone It therefore became fastened in the periosteum where it was not a safe fixed point for measuring purposes (cf *Lacroix 1950*) To insert the indicator reliably in the humerus diaphysis a small operative exposure of the bone surface seemed necessary This however could be sufficient trauma to cause growth disturbance and furthermore could hardly be thought defensible on ethical grounds *There was always the possibility that the presence of a steel pin in the middle of the* diaphysis could have some slight effect on the growth (*Tapp* 1966 *Hansson* 1967) The experiments were therefore abandoned

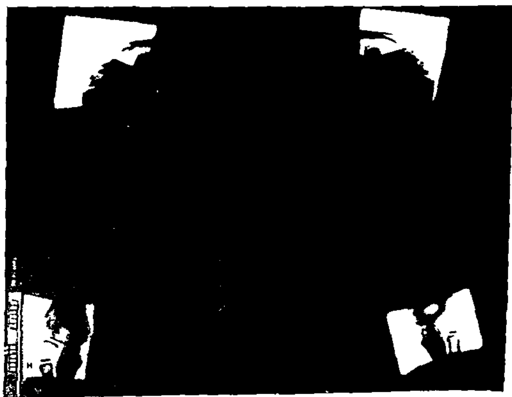


Fig 9 Orthodiagraphic x ray picture for measurement of humerus

The humerus measurements were made with a ruler on the rontgen pictures (Fig 9) against the light they were made twice and sometimes three times at first by an assistant and then by the author The measuring values were usually identical or could show a difference of at most 1 mm

This agrees quite well with earlier indication of the measurement error of 1 mm At correctly performed rontgen examination this error is entirely conditioned by the impracticability of measuring more accurately than 1 mm even on a rontgen picture of good quality

Correction motivated by faulty adjustment of the central beam was made in conjunction with the author s measurement but was necessary in rather a few cases because an error of this nature is normally observed at the rontgen examination and would result in a new and more accurate picture being taken

Occasional absurd measurement values such as length reductions occurred and were attributed to movements made by the patient between the exposures Such values were excluded at the statistical treatment

C Statistical methods

The character of the clinical material caused the statistical working model to be of the same type as that used at the appraisal of the experimental material in *Part Two* Thus a comparison between fractured bone and control bone was made for each patient However, because the measurements were made at irregular time intervals, *difficulties arose at the* formulation of universal working models in mathematical symbols In principle however, the difference

$$d_{ij} = (X_{Fi\,(j+1)} - X_{Ci(j+1)}) - (X_{Fij} - X_{Cij}) \text{ where } \begin{array}{ll} i = 1, 2, 3 & n \text{ (patients)} \\ j = 1, 2, 3 & n \text{ (measuring time)} \end{array}$$

is valid

X_{Fij} is the measuring value for the fractured bone in the i^{th} patient after the j^{th} measuring occasion X_{Cij} is the measuring value for the control bone in the i^{th} patient after the j^{th} measuring

The analysis was rendered difficult by the variable of the bone length before fracture being completely unknown In agreement with the planning of the clinical investigation the statistical analysis was thus limited to measurements after the fracture, where the first measurement in most cases took place three months after the trauma

The purpose of the analysis was an estimate of the size of the added growth on the fractured side and an estimate of the time for maximum overgrowth Successive differences were established here between consecutive measuring occasions The method was constructed so that an answer could be expected to the question of when a possible overgrowth is recordable in time and in such a way that it was possible to estimate the total average increase in growth either for the fractured side or for the control side

Statistical formulae and symbols

The statistical analysis was made by conventional methods whereby the following formulae were preferably used

$$s = \sqrt{\frac{\Sigma(x - m_x)}{n-1}} \qquad t\,(n-1) = \frac{m - \mu}{s/\sqrt{n}}$$

$$m_d - t_{p\%}\,(n-1)\frac{s_1}{\sqrt{n}} < \mu < m_d + t_{p\%}\,(n-1)\frac{s_1}{\sqrt{n}}$$

$$t\,(n_1 + n_2 - 2) = \frac{(m_1 - m_2) - (\mu_1 - \mu\,)}{s\sqrt{\frac{1}{n_1} + \frac{1}{n}}}$$

$$\text{where } s = \sqrt{\frac{(n_1 - 1)\,s_1 + (n_2 - 1)\,s}{n_1 + n\ - 2}}$$

Abbreviations

m = arithmetic mean
df = degrees of freedom
MS = mean square
t = Student s t distribution
p = probability

s = standard deviation
SS = sums of squares
u = standard normal distribution
F = Snedecor s F distribution
P = per cent

Used levels of significance

(—) insignificant
(*) almost significant
(**) significant
(* *) highly significant

C Statistical methods

The character of the clinical material caused the statistical working model to be of the same type as that used at the appraisal of the experimental material in *Part Two* Thus a comparison between fractured bone and control bone was made for each patient However, because the measurements were made at irregular time intervals, difficulties arose at the formulation of universal working models in mathematical symbols In principle, however the difference

$$d_{ij} = (X_{Fi(j+1)} - X_{Ci(j+1)}) - (X_{Fij} - X_{Cij}) \text{ where } \begin{array}{ll} i = 1, 2, 3 & n \text{ (patients)} \\ j = 1, 2, 3 & n \text{ (measuring time)} \end{array}$$

is valid

X_{Fij} is the measuring value for the fractured bone in the i^{th} patient after the j^{th} measuring occasion X_{Cij} is the measuring value for the control bone in the i^{th} patient after the j^{th} measuring

The analysis was rendered difficult by the variable of the bone length before fracture being completely unknown In agreement with the planning of the clinical investigation, the statistical analysis was thus limited to measurements after the fracture where the first measurement in most cases took place three months after the trauma

The purpose of the analysis was an estimate of the size of the added growth on the fractured side, and an estimate of the time for maximum overgrowth Successive differences were established here between consecutive measuring occasions The method was constructed so that an answer could be expected to the question of when a possible overgrowth is recordable in time and in such a way that it was possible to estimate the total average increase in growth either for the fractured side or for the control side

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2 *Fract coll chir humeri*

This includes 18 cases 7 dislocation grade +, 11 grade + + Of the patients 15 (83 3 %) show an obvious added growth (more than 2 mm) on the fracture side The average final growth increase in category + + is 9 0 mm (maximum value 21 mm) and for category + 6 8 mm (maximum value 13 mm)

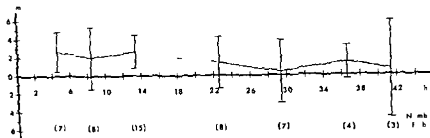


Fig 10 Average overgrowth in mm during consecutive time intervals in humerus after fracture of the surgical neck Dislocation + and + +

At a study of the development of growth increase in relation to time (fig 10) almost significant overgrowth is found approximately 4 months after the occurrence of the fracture and a possible maximum around 12 to 16 months In the continued progress the curve lies above the x axis continuously until about 40 months have elapsed but statistical significance no longer exists then therefore nothing definitely can be said about the time point for the cessation of growth stimulus

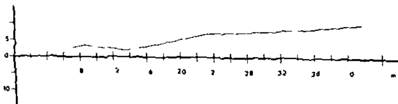


Fig 11 Acc mulated overgrowth in mm in humer s after fracture of the su g cal neck D slocation + and + +

At calculation of the average accumulated growth increase (fig 11) a final value of 8 3 mm is found after 40 months There is no tendency to regress but this cannot be considered altogether excluded on statistical grounds

4

CHAPTER IV

RESULTS

A Analysis of the growth reaction on fracture

In the following account, the fractures are distributed on four different categories

1 Fract diaphys humeri, dislocation grade + and ++
2 Fract coll chir humeri dislocation grade + and ++
3 Fract supracond humeri, dislocation grade +
4 Fract supracond humeri, dislocation grade ++

The classification according to dislocation, as given in Table 2, is thus partly relinquished It is obvious that a considerably larger number of cases would have made it possible to retain this original classification for all fracture types With the present material, however no meaningful statistical analysis would be possible if categories 1 and 2 above with 18 and 8 representatives respectively were further divided

1 Fract diaphys humeri

The material on this fracture level includes only 8 patients 7 with dislocation grade ++ and 1 with grade + No possibilities for statistical analysis exist here, and graphic representation has not been judged practical either It can merely be established that all the patients show obvious overgrowth (more than 2 mm) which in 3 cases 21 to 26 months after the fracture reveals a limited tendency to reduce Average final overgrowth for the 7 cases of dislocation grade ++ is 7 4 mm (the highest value 12 mm) whereas the patient with dislocation grade + has an overgrowth of 5 mm This difference hardly allows any conclusions concerning the influence of the dislocation on the growth increase

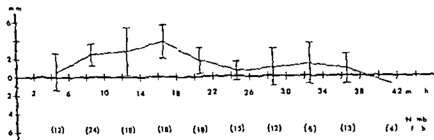


Fig 14 Average overg owth in mm during consecutive time intervals in humerus after s pracondylar fracture Dislocation + +

in some of the growth curves in *Part Two* (cf p 00) Thus it cannot be excluded that this tendency to a second growth spurt unconvincing as yet does represent a reality where the physiological substratum is unknown

The existence of a tendency to growth retardation contributes to the value of accumulated average growth increase (Fig 13) being small 1 1 mm at the end of the 38th month Corresponding value after 18 months on the other hand is 3 3 mm (individual maximum value 7 mm) For more exact comparison with other fracture categories it would of course have been desirable to adjust the measuring values to the 40th month here too but the composition of the material did not allow this

4 Fract supracond humeri dislocation grade + +

The material consists of 33 cases of which 30 (90 9 %) show obvious growth acceleration Significant growth increase (Fig 14) can be established

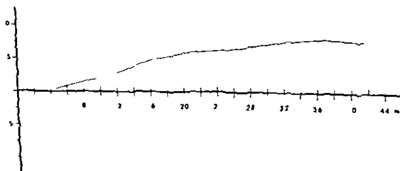


Fig 15 Acc mulated overgrowth in mm in humer s after supracondylar fracture Disloca tion + +

3 Fract supracond humeri dislocation grade +

Out of 27 patients, 17 (63 0 %) show obvious added growth in the fractured bone from 9 to 18 *months* after the injury The growth in relation to time (Fig 12), is almost significantly increased in the time interval 9—14

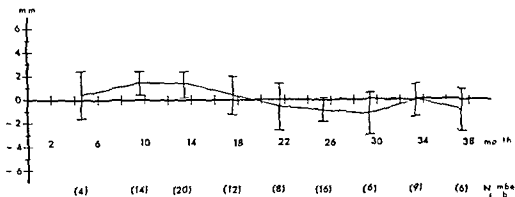


Fig 12 Average overgrowth in mm during consecutive time intervals in humerus after supracondylar fracture Dislocation +

months, with a probable maximum at approximately 12 months after the fracture Between 22 and 30 months after the trauma, a slight tendency for comparatively more rapid growth appears in the control bone, but this phenomenon is not statistically guaranteed at any time Although such growth retardation, real or relative is registered in 11 cases — if 2 mm is accepted as proof of regress — a considerably larger material is needed to confirm the reality of such a phenomenon

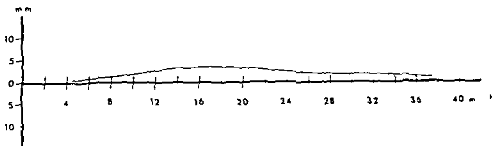


Fig 13 Accumulated overgrowth in mm in humerus after supracondylar fracture Dislocation +

Another observation with even less statistical foundation is a slight tendency to a second growth spurt ocurring about 30 to 36 months after the fracture and noted in 6 cases That such a doubtful observation is mentioned at all is explained by its occurrence in the other growth diagrams in this chapter and besides — actually with slight statistical significance —

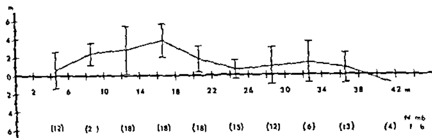


Fig 14 Average overgrowth in mm during consecutive time intervals in humerus after supracondylar fracture Dislocation ++

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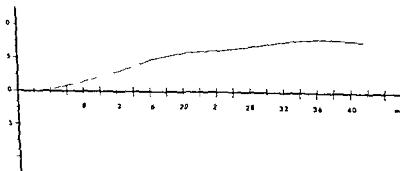


Fig 15 Acc m lated overgrowth in mm in humerus after supracondyla f act re Dislocation ++

approximately 8 months after the fracture and is maintained to the 21st month, with a probable maximum in the interval 16—18 months Even 2 years or more after the injury, the curve still lies above the x axis, but without statistical significance, which can be interpreted as a slight tendency for continued growth acceleration up to 3 years after the trauma The accumulated average increase in length in the fractured bone during the time 0—40 months amounts to a final value of 8 8 mm (individual maximum value 18 mm) (Fig 15), thus very considerably more than in the previous category A slight tendency to growth retardation — whether true or relative — in the fractured bone during the third year, such as was mentioned in the previous fracture category could be registered in 8 cases but as before with no statistical significance Its influence on the final accumulated overgrowth was accordingly practically nil A second growth acceleration, equally insignificant, was observed in two cases

B Other statistical analysis of the clinical material

Adjus ment of a curve indicating growth of the control bone (for the time being regarded as representative of normal humerus growth) was made with the method of least squares where the material was arranged in intervals of 1 year and consideration given to the localization of the measuring occa sions in each annual interval (Fig 16) The almost parallel course of the dotted lines (giving a confidence interval of 95 %) in close relation to the en al c a ve ndicates good statistical reliability in the age interval 5—15 years

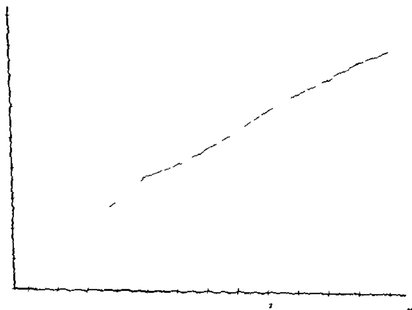


Fig 16 G owth of co t of h merus

Attempts were also made to appraise whether different intensity in the growth acceleration exists in different ages Because of the limited scope of the material it was here necessary to work with all the fracture types combined Because an increase of a few mm in length in a 2 year old child can imply equally large or larger relative added growth than 1 cm in a 10 year old the total length of the bone has been taken into account at the

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CHAPTER V

DISCUSSION

Faced with a compilation and evaluation of the results we may now recapitulate the original problems and the present standpoint of growth studies for which the reader is referred to pp 10 and 22 Here the problems posed by the author are surveyed point by point

1 Is growth stimulus after fracture in long bone a constant phenomenon?

A question of this nature concerning measurements — comparatively good but none the less of limited accuracy — of biological material cannot be expected to be given a 100 % positive answer It is important here to determine when overgrowth is considered to occur and this is a matter that must be set in relation to method and method error The question is also whether the problem is to be viewed from a strictly theoretical or a clinical aspect If the problem is regarded practically clinically which is the case here mm accuracy is enough and thus the measurement method used is satisfactory

It might now be objected that differences in length between the upper arms are of no practical importance and that a clinical view of this phenomenon is meaningless As opposed to this however it can be said that the results obtained for humerus could in principle be applied to both femur and tibia in which difference in bone length is a real clinical problem

To return to the above stated problem and with reference to figures for substantial overgrowth (>2 mm) given in the previous chapter it can be established that 70 out of the 86 cases in the material showed such an increase in growth i e 81 % From a clinical standpoint this result at a general application would mean that measurable difference in bone length after fracture in growing long bone cannot be expected in every instance although most often and that the frequency of this — according to this material to the method used here and limited to humerus — lies around 80 % It is not altogether certain that conclusions concerning growth in other long bones can be drawn from the results of this investigation particularly not if essential anatomical and/or physiological differences exist

calculations The investigation was made with covariance analysis and division into both 3 and 2 age groups was tried, but in no instance did it give significant differences

The total fracture material was compiled in a diagram (Fig 17) analogous to those made for the various fracture types Such a compilation must,

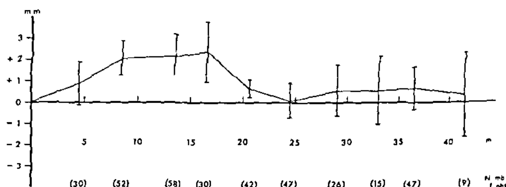


Fig 17 Average overgrowth in mm during consecutive time intervals in humerus estimated for the whole present fracture material and both degrees of dislocation

of course, be taken with considerable reservation The development of the growth stimulus accords largely with that indicated for the separate fracture types but the significance is higher during the period 8—21 months (cf Table 4) Although statistically insignificant the development of two humps in the growth diagram is slightly more pronounced here

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between humerus and such bones Factors of special importance in this connexion might be circulatory conditions, arrangement of growth plates normal growth curve for the bone in question, &c Although no fundamental differences of this kind exist between different long bones these reservations none the less suggest that on purely logical bases it is not justified to conclude that all long bones must show overgrowth in approximately the same frequency Clinical experience, such as has been given by the authors mentioned in the historical account, suggests that overgrowth most often occurs in femur and next in tibia *Calati & Poli* (1959) estimate the frequency of obvious growth stimulus at diaphysis fracture in femur to be 63 6 % in tibia 60 %, in humerus *27 7 %*, and *radius + ulna 14 3 %* These authors point out however, that the real frequency figures are probably higher The relation between the figures for the various long bones must also be questioned that femur thus has a growth acceleration frequency more than twice as high as humerus ought in all probability to be reflected in some essential difference in the construction of these two bones and this cannot possibly be However, the fact that femur normally has a higher growth rate than humerus can have played some role in this connexion

But if we accept the information from the above mentioned authors that femur and tibia fractures more often than humerus fractures are accompanied by increase in growth and if the frequency of growth acceleration in humerus in accordance with the present author s results is approximately 80 %, it would suggest that fractures in the lower extremities almost always result in overgrowth Here a factor enters through which the fractures of the bones are not directly comparable It must be taken into account that investigations made so far of the growth stimulus concerning femur and tibia almost exclusively referred to diaphyseal fractures which at least in the matter of femur often show considerable dislocation with accompanying larger periosteal lesion haematoma formation &c

2 a Does the growth stimulus vary with the dislocation grade of the fracture?

As already mentioned *Barfod & Christensen* (1958) and *Hjort Guldhammer* (1963) noted especially strong increase in growth after severely dislocated fractures *Blount* (1944 1950 1954) *Blomquist & Rudstrom* (1943) *and others point* out that operated fractures (which initially must usually have been considerably dislocated and where moreover the operation trauma results in further periosteal lesion haematoma formation &c) are followed as a rule by strong overgrowth *Lezander* (1929) and others

on the other hand have not found any obvious relation between growth increase and dislocation Most investigators in recent years have thus found that in this respect there is a positive correlation

In the present author s material statistical significance exists concerning the difference in overgrowth between categories 3 and 4 p 47 (supra condylar fractures dislocation grade + and ++)[1] The values for average accumulated overgrowth are most marked after 40 month 1 1 mm for category 3 8 8 mm for category 4 The investigation of the development of growth increase with respect to time (diagram 1 and 5) shows an obvious difference with values that are almost significant in category 3 and highly significant in category 4 It must thus be considered certain that moderately or severely dislocated supracondylar humerus fractures show an essentially higher growth acceleration than do non dislocated for which however there is a statistically verified growth increase although only slight

Even though corresponding appraisal of the factors in diaphyseal and surgical neck fractures cannot be given statistical significance it must none the less be pointed out that of 8 and of 15 cases repectively with marked added growth only 2 belong to dislocation grade + Here too a similar tendency can be discerned regarding the importance of the dislocation in these fracture types to what has just been said about the supracondylar fractures

The present investigation does not explain or even indicate what causes this difference in growth reaction A larger dislocation implies a greater vessel lesion periosteal lesion injury to soft parts consequently a more intense reaction from surrounding tissues and a longer period of repair but which of these factors plays the decisive role here is an open question That the positive correlation between dislocation and overgrowth must generally refer to all long bones eems to be beyond doubt This factor has — with a high degree of probability — been shown partly to apply to three fracture types in one and the same bone and partly to agree with several clinical and scientific reports concerning femur and tibia (*inter al* *Blount* 1954 *Barfod & Christensen* 1958 *Calati & Poli* 1959 *Goff* 1960 *Hjort Guldhammer* 1963)

From what is mentioned above it now seems understandable that the femur diaphysis fractures which are most often severely dislocated and with overlapping ends practically always produce an increase in growth

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[1] Observed alue of th test function t=3 68 21 deg ees of freedom

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supracondylar fractures which however is outweighed by some cases with slight or no growth acceleration

ad β) As already explained in Chapter III there was no practical possibility of solving this problem by inserting an indicator in the diaphysis as a fixed measuring point Measurements of patients around puberty during the years immediately before and after the disappearance of the distal growth plate were too few to allow even a rough estimate Otherwise this is a time when at first two and later only one growth plate is in function from a large material of this age it could be possible to gain some information about this problem

2 c Does the growth stimulus vary with age?

A comparatively large increase in growth in children up to 4 years of age was observed by *Blomquist & Rudstrom* (1943) whereas *Barfod & Christensen* (1958) *Hjort Guldhammer* (1963) *Murayama* (1963) and to some extent also *Hedberg* (1944) hold that overgrowth is scanty during the 3—4 first years of life Actual statistical significance in support of one or other view was not produced by these authors

No positive significant difference between different age groups was found in the present author s investigation irrespective of whether the material was distributed into 2 or 3 categories It must be pointed out that the increase in growth at this analysis was not calculated in absolute figures but as a percentage of the bone length Earlier investigators on the other hand have employed absolute figures (*Hedberg* 1944 *Barfod & Christensen* 1958 *Hjort Guldhammer* 1963)

Not only the size of the growth stimulus but also its duration in various ages could be valuable to investigate With regard to the fact that the fracture healing process runs its course more rapidly during the first years of childhood and that the growth stimulus has been thought to continue as long as the consolidation of the fracture and the final reconstruction of the fractured bone are in progress (*Ollier* 1867 *Trueta* 1953 *Goff* 1960 and others) it would be reasonable to find a shorter duration for overgrowth after fracture during the first years of life It is possible that the growth acceleration is more rapid in the youngest but acts for a shorter period

Fig 16 (growth of the control bone) which is supposed to show normal growth of the humerus (the implicit reservation is induced by observations in *Part Two* concerning growth disturbance in the control bone cf p 90) and in any case is not likely to deviate much from the

whereas the humerus fractures with highly varied position and dislocatio grade produce a lower frequency of overgrowth

2 b Does the growth stimulus vary with the distance of the fractures fro the growth regions?

In chapter I (p 13) is stated that the growth potential is 3—4 time *higher within the proximal humeral growth plate than in the distal plat* It may now be reasonable to assume that a fracture close to the growt plate with the higher potential has a different growth stimulating effe than a fracture just midway between the growth plates or one close to th plate where growth normally is slower To estimate this not merely measu rements of the development of the total humeral length but als ascertaining of the growth increments from each cartilage plate should be o importance Accordingly, question 2 b becomes subdivided in two part namely

α) Does the total overgrowth vary with the site of the fracture?

β) How do the two growth plates of humerus react upon fractures a different levels?

ad α) *From the previous part of the discussion it is clear that the degree o dislocation* is an important factor when considering overgrowth Thus, it i *here necessary to compare only* fractures with similar amount of displace ment It is a truism to state that this is difficult What two fractures hav the same displacement? Nevertheless in the categories 1 and 2 on pp 47— 48 fractures of dislocation degree ++ are seperated — and their average final growth given — while category 4 p 50, solely consists of such cases With due reservation a comparison may be attempted *It then* appears that average final overgrowth amounts to

in diaphyseal fractures, dislocation ++	7 mm
in fractures of the surgical neck, dislocation ++	9 mm
in supracondylar fractures dislocation ++	9 mm

From these values reliable conclusions are not to be drawn The differen ce appearing between on the one hand metaphyseal, on the other diaphyseal *fractures* is definitely insignificant esp considering the small numbers for the shaft fractures If the individual cases are scrutinized there may be noted a small preponderance for strong overgrowth (>10 mm) among the

supracondylar fractures which however is outweighed by some cases with slight or no growth acceleration

ad β) As already explained in Chapter III there was no practical possibility of solving this problem by inserting an indicator in the diaphysis as a fixed measuring point Measurements of patients around puberty during the years immediately before and after the disappearance of the distal growth plate were too few to allow even a rough estimate Otherwise this is a time when at first two and later only one growth plate is in function from a large material of this age it could be possible to gain some information about this problem

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A comparatively large increase in growth in children up to 4 years of age was observed by *Blomquist & Rudstrom* (1943) whereas *Barfod & Christensen* (1958) *Hjort Guldhammer* (1963) *Murayama* (1963) and to some extent also *Hedberg* (1944) hold that overgrowth is scanty during the 3—4 first years of life Actual statistical significance in support of one or other view was not produced by these authors

No positive significant difference between different age groups was found in the present author s investigation irrespective of whether the material was distributed into 2 or 3 categories It must be pointed out that the increase in growth at this analysis was not calculated in absolute figures but as a percentage of the bone length Earlier investigators on the other hand have employed absolute figures (*Hedberg* 1944 *Barfod & Christensen* 1958 *Hjort Guldhammer* 1963)

Not only the size of the growth stimulus but also its duration in various ages ould be valuable to investigate With regard to the fact that the fracture healing process runs its course more rapidly during the first years of childhood and that the growth stimulus has been thought to continue as long as the consolidation of the fracture and the final reconstruction of the fractured bone are in progress (*Ollier* 1867 *Trueta* 1953 *Goff* 1960 and others) it would be reasonable to find a shorter duration for overgrowth after fracture during the first years of life It is possible that the growth acceleration is more rapid in the youngest but acts for a shorter period

Fig 16 (growth of the control bone) which is supposed to show normal growth of the humerus (the implicit reservation is induced by observations in *Part Two* concerning growth disturbance in the control bone cf p 90) and in any case is not likely to deviate much from the

normal curve, shows that the growth more or less runs its course not far from linearly between the ages of 4 and 15 years This could support to some extent the concept held by *Blount* and others that the growth stimulus after fracture varies little in the mentioned age interval

At investigation of the importance of the age factor, the skeletal age should by rights be determined and used as basis for the appraisal Rontgenological material (pictures of hand skeleton) for such calculations however, was not available to the author The developmental level of the bone nuclei in both ends of humerus provides no basis for sufficiently accurate determination of skeletal age

3 How soon after fracture can growth stimulus be demonstrated, and when does it terminate?

As explained in the previous chapter, it was not possible to give the exact time for the appearance of measurable growth increase The earliest recording that can be allotted any statistical significance refers to the fractures in the surgical neck and was made within approximately 4 months after the injury The progress before that is not sufficiently mapped to allow any statement whatsoever

Observation of the curves for the growth acceleration in relation to the number of months since the injury (see Fig 10 12, 14) gives an indication of the time for the maximum increase in growth This maximum is most pronounced for the supracondylar fractures of dislocation grade + +, where it occurs 16—18 months after the injury Its appearance is more vague in supracondylar fractures of dislocation grade + where it occurs 12 months after the injury, and in *collum chirurgicum* fractures where the interval is 12—16 months With reservation for the fact that nothing is known about the growth acceleration during the first 4 months it can thus be maintained *that a maximum occurs 12—18 months after the fracture This phenomenon* does not appear to have been accurately recorded earlier To what extent in coincides with any phase in the consolidation of the fracture or in the vascular post traumatic reaction is a problem not contained in this investigation

The termination of statistically significant increase in growth for dislocated supracondylar fractures occurs at 21 months for non dislocated *fractures* at 14 months and for *collum chirurgicum* fractures approximately 16 months after the injury The curves however do not reach zero position at the mentioned times For the first mentioned fractures the average values of increase in growth lie somewhat above the x axis until

fully 36 months after the injury, and almost the same condition applies to the *collum chirurgicum* fractures This might be interpreted as a limited tendency to persistent overgrowth in the fractured bone

Contrary to this the curve for non dislocated supracondylar fractures intersects the x axis at 20 months and thereafter shows for at least one year a slight tendency to negative values in other words a higher growth rate for the control side whether this is due to acceleration of the growth in uninjured bone or to retardation in fractured bone These statistically not guaranteed slightly negative values for average growth per time interval partly condition the insignificant accumulated growth of the non disloca ted supracondylar fractures At the time when the curve goes below the x axis the average total growth is 3 5 mm but thereafter slowly reduces to the final value 1 1 mm mentioned before

No doubt there is a similarity between the diagrams for the development of growth acceleration in dislocated supracondylar fractures and fractures through the surgical neck while the corresponding curve for non dislocated supracondylar fractures is not only flatter but also remains on the positive side for a much shorter time In what other respect then are the two first mentioned fracture categories mutually comparable and different from the lastmentioned group? It seems probable that the dislocation grade plays a role here too Of the 18 fractures through the surgical neck 11 belong to grade + + i e 61 % This relative majority for dislocated fractures might be reflected in a development of the growth acceleration similar to that in dislocated supracondylar fractures Hypothetically and with emphasis on the fact that the parts of the curves which lie beyond 18—20 months lack statistical significance it could be postulated that the duration of growth stimulation is correlated to the amount of dislocation This appears to be a justifiable statement because there is reason to suppose that the reparative processes in the bone require far longer time after a severely dislocated fracture than after a fracture in exact position and this remodelling is generally assumed to concur with the process of overgrowth Already *Ollier* (1867) thought that the reopening of the medullary cavity would coincide with the disappearance of the growth stimulus a theory which *Trueta* (1953) has emphasized The so-called medullization must obviously be a much slower process when the fracture ends are widely displaced or overriding than when the contact is close.

4 Are there signs of equalization of bone length difference produced by fracture during the continued course of growth?

Individual observers have noted a more or less pronounced tendency to equalization of post traumatic bone length difference *L Bohler* (1954) states that these length discrepancies are transient *M Brattstrom* (1963) who investigated children with rheumatoid gonarthritis, found with rontgenological measurements a moderate increase in growth on the diseased side, which was eliminated, however, during the course of one or two years

The only factor in the present material that might argue for a regress in part of the overgrowth is the statistically nonsignificant negative values of increase in growth 2—3 years after non-dislocated supracondylar fracture In some isolated cases of dislocated supracondylar fractures similar observations were also made *This highly uncertain observation is hard to ex*plain, especially as it cannot be determined whether it is a question of retardation of the fractured bone or of acceleration of the control bone In the case of mechanical traumata, *Blount* (1954) has found that the growth plate nearest to the fracture ceases to function somewhat earlier than normally which probably argues for a lower growth rate during the immediately previous period This can to some extent (fracture cases near the puberty) be the cause of the mentioned uncertain negative growth values 2—3 years after a fracture

PART TWO

Experimental Study of Growth Reactions from Proximal and Distal Growth Regions After Cortical Drilling

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CHAPTER VI

STIMULATION OF LONGITUDINAL BONE GROWTH BY EXPERIMENTAL TRAUMA REVIEW OF LITERATURE

The various operations that are performed clinically to increase the longitudinal growth locally in a bone have most often been tested before hand on experimental animals mostly rabbit therefore a copious literature exists in which the effects of various forms of trauma to bone tissue and periosteum have been investigated in animals A variant of this the placing of different organic or inorganic substances in the medullary cavity or metaphysis however is only indirectly related to the theme of this investigation (cf *Langenbeck* 1869 *Meisenbach* 1910 *Kor gsweser* 1925 *Trout* 1915 *Bohlman* 1929 *Bergmann* 1931 *Kishikawa* 1936 *Wu & Miltner* 1937 *Chapchal & Zeldenrust* 1948 *Bertrand & Trillat* 1948 *Pease* 1952 *Wilson & Percy* 1956 *Haas* 1958 *Nordentoft & Guldhammer* 1964 and others) For placing the various materials in the bone some form of fenestration or drilling through periosteum and cortex is of course required and the reports do not allow any positive judgement whether the recorded often insignificant or inconstant increases in growth are due to traumatization of bone (periosteum) or to the presence of a foreign body or to both Because these experiments are not purely traumatic they are left out here

A *Periosteal strippings*

Ollier (1867) removed the periosteum from the tibia diaphysis in a series of rabbits Three months later he could record an elongation of the operated bone of 2—5 mm Similar experiments do not appear to have taken place until *Wu & Miltner* (1937) reported a series of stimulation experiments on 22 rabbits which included periosteal stripping of varying extent During the course of 3 months 19 of the 22 developed a considerable overgrowth in the operated bone of from 5—15 % of the total length The experiments were repeated by *Lacroix* (1951) who obtained a clear reaction in 7 out of

5

PART TWO

INTRODUCTION

With clinical material and rontgenological investigation, the first part of this work has provided much information of a high degree of probability concerning growth stimulation in various types of fractures in *homo* and the information obtained has satisfactorily answered most of the problems. When the experiments with insertion of diaphyseal metal indicator were abandoned (p 43), it was impossible to determine the relative growth proportion from proximal and distal growth region after fracture, and because of the limited material, it was also impossible to judge whether different fracture level gave different growth stimulus (problem 2 b p 000) With the object of gaining better information on this point an experimental investigation was added where traumatization of long bone in growing rabbits was carried out The investigation method in the present part is in many respects based on a work published by *Hansson* (1967) Daily Growth in Length of Diaphysis Measured by Oxytetracycline in Rabbit Thus the same intravital labelling method and the same preparation technique was used and the fluorescence microscopical investigation was made with the same optical equipment For this reason the description in some sections could be given summarily and for complementing details the reader is referred to the very detailed work just mentioned

B Drilling through the metaphyseal cortex into the medullary cavity

As mentioned earlier, metaphyseal drilling was tested clinically by *Ferguson* (1933) and the report of it probably induced *Kishikawa* in 1936 to perform similar drillings in an unknown number of rabbits A few weeks later he could establish rontgenologically growth increase in most of the experimental animals *Compere & Adams* in 1937 continued along the same lines and drilled holes in the femur of rabbits in the two metaphyses as well as in the centre of the diaphysis in one and the same bone Ten weeks later no measurable increase in length could be established However only 6 experimental animals were used *Hutchison & Burdeaux* (1954) besides stasis experiments also performed drillings out of 10 dogs 5 showed overgrowth

Common to the stimulus experiments mentioned here is that the number of the experimental animals was too small that the measuring method was hardly precise enough and that the localization of the drillings was not reported with any degree of accuracy *Hansson & Wiberg* (1963) and *Wiberg* (1964) used drilling more systematically and in larger series In an experimental series where 16 rabbits were used drilling was carried out with dental drill (diameter 2 mm) both in the distal femur epiphysis and in the proximal tibia metaphysis In two other series of 17 and 14 rabbits respectively drilling was performed in the proximal tibia metaphysis only During the following period of 2 months the animals were sacrificed and the length of tibia was determined with the aid of 0 1 mm—graduated calipers A growth increase of up to 1 0 mm was recorded in all series The experiments however were mainly intended to discover possible post traumatic reaction in the proximal growth cartilage of the tibia which was studied microscopically in all experimental animals The number of cells in the cell columns of the proliferative zone were found to decrease during the days immediately after the drilling and the whole of this zone reduced in height as did the entire growth cartilage In general no definite changes could be found in the hypertrophic layer However this investigation did not permit any positive conclusions concerning whether this reduction of the growth cartilage was related to increased or retarded growth rate because the recording of the growth referred to the total growth increase of tibia

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C Experimental fractures and osteotomies

Growth studies made with the aid of experimental fractures and osteotomies are reported frequently in the literature One of the earliest was made by *Levander* (1929) During his clinical investigations he had as mentioned (p 17) observed that increase in length of tibia could occur after femur fracture which was investigated in closer detail experimentally with rontgenological measuring technique *Levander* began by investigating ani o melia in rabbits but could not demonstrate any of importance Thereafter 13 artificial fractures of tibia were described In 11 of these experimental animals *Levander* could prove increase in length of femur Moreover 5 femur fractures were also made and here positive increase in length in tibia was found in 1 rabbit and uncertain increase in 3 The reaction of femur to tibia fracture was observed to be considerably stronger than reaction of tibia to femur fracture *Levander* also noted that the increased growth reaches a certain maximum and is then inclined to slow down The author did not mention precisely where the fractures were situated However they were made with percutaneous breaking in the middle of the diaphyses In 1936 *Bisgard* and in 1937 *Bisgard & Martenson* reported experiments carried out with goats Diaphyseal fractures were made and then controlled with repeated rontgenological measurements The fractures were transverse with or without over riding position and in both cases resulted in small growth increase of a few mm

Compere & Adams in 1937 published several different series of experiments with growth stimulus including diaphysis fractures among others These had actually been made with the object of finding out positively — with the aid of them and of indicators placed on each side of the fracture — whether interstitial growth occurs at healing No such growth could be demonstrated in rabbit but increased longitudinal growth was noted as secondary finding in fibula at fracture of tibia a phenomenon attributed to the regional post traumatic hyperaemia The authors who also experimented by drilling holes as well as with complete fractures found that the former as distinct from the fractures gave no measurable growth increase They therefore presumed that dislocation could be of importance for the development of overgrowth

Greville & Janes in 1957 published a report of experimental fractures in puppies where growth increase was accounted for in all instances This

A similar experimental trauma was used by *Hansson* (1967) in his investigation of the growth in rabbit tibia after different types of skeletal trauma Here, too, drilling was performed, but the hole was made about 5 mm in diameter and was located 8—10 mm below the proximal growth plate of tibia With this type of drilling, intentional destruction of the medulla, level with the drilled hole, was also made with the aid of the drill Plugging was then carried out with homologous bone, as earlier suggested by *Trueta* (1953, 1958) and used clinically by among others *Stahl* (1957) This so called plugging is done by packing the medullary cavity *level with the drill hole with homologous bone, whereby the vascular* branches from *a nutritia* are expected to be completely destroyed Growth determinations were then made with tetracycline technique (for details, see *below) These determinations showed that traumatizations of the type* described here resulted in slight stimulus in the proximal growth plate and a considerably more powerful stimulus in the distal in the operated long *bone, compared with the contralateral* Similar reaction was obtained after drilling with medullary cavity destruction, but without plugging, whereas merely drilling and avoiding medullary lesion resulted in about the same growth stimulus in the two growth cartilages in the operated bone The stimulus in the proximal growth region, whose medullary vessels were in this case intact, was thus more pronounced than after the previously mentioned operations Corresponding reaction was found to a lesser degree also at only periosteal incision

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series also seemed to provide evidence for the opinion that the growth acceleration was most marked where there was obvious dislocation In Sweden, *Blomquist & Rudstrom* in 1943 carried out experiments that were fairly identical with those reported by *Compere & Adams* and obtained similar results *Wray*, who with different co workers studied the vascular reaction to fracture at the end of the 1950s, showed together with *Goodman* in 1961 that *it is possible at diaphysis fracture in rat tibia to establish a* temporary halt to the growth in femur, not only on the same side but also *in the contralateral extremity This however, in a short time changes into accelerated growth bilaterally, although mostly on the fracture side In* 1965 *Yabsley & Harris* investigated the effect that closed fractures in rabbit tibia could have on the blood supply to the growth plate, and in passing, recorded an increase in length after these fractures

To summarize the survey of the literature given here has shown that increase in growth is obtained both after periosteal stripping, after drilling the medullary cavity, and after fracture (osteotomy) Bases have been found for the supposition that the extent of the growth acceleration is related to the degree of severity of the dislocation It was observed more over that trauma to a long bone in an extremity can affect the growth rate in other bones in the same extremity

Finally, some investigators have noted that a trauma in the vicinity of the proximal growth region of a long bone triggers off increased growth not appreciably from the adjoining growth plate, but from the distal

CHAPTER VII

MATERIAI

Most experimental growth studies seem to have been carried out on rabbit although chicken rat guinea pig pig goat dog have also been used (cf reviews by *Taillard & Morscher* 1965 *Hansson* 1967, *Sunden* 1967) The advantage of using rabbit is its rapid growth moreover its long bones contrary to rat and guinea pig are large enough to allow operative measures *Hansson* (1967) developed a method for exact growth determination and mapped the normal growth in rabbit it therefore seemed fitting to use rabbits for this part of the present author s studies

Litters of white rabbits supplied from two different sources were used They were aged about 4 weeks when delivered without mother to the animal depot Thereafter they were observed for some days before the experiments were performed The weight of those that seemed healthy varied from 300 to 600 gm at the beginning of the experimental period i e aged approximately 30 days They were fed with vitaminized nutritive preparations in the form of pellets (Ewos) and water They were housed in cages made of wire-netting with floors of the same material in a room with daylight where the temperature was 16—18° C and the relative humidity 40—50 %

609 rabbits were used of which 205 were discarded for various reasons The largest loss was caused by unsuccessful preparations of sections for growth determinations the next by lethal enterocolitis and finally deaths occurred in connexion with the operations

Occasional instances of diarrhoea occurred probably caused by slight enterocolitis but as long as these symptoms had no obvious negative effect on the body weight of the animals (recorded both at the arrival and at frequent intervals during the experimental period) such a slight disorder was not considered sufficient to disqualify the animals (cf *Persson* 1968)

CHAPTER VIII

METHODS

A Notes on the choice of methods

At the start of the experimental studies, three questions were posed

1 What stimulation methods should be employed?

2 In which bones, and where on them, should the growth stimulating method be applied?

3 What measuring method should be used?

Ad 1) What was desired, was a fracture or a trauma as similar to a fracture as possible Causing a fracture by breaking a long bone without exposing it was of course a simple measure (cf *Levander* 1929, *Compere & Adams* 1937), but it would not be possible to place it with desirable anatomical precision and the degree of dislocation and possible splintering could vary considerably It could also be presumed that an experimental animal so treated would not put weight on the damaged bone (radius, however, is an exception, cf below) and the withdrawal of the pressure of the body weight could be expected to have some effect on the growth Several studies (*Ollier* 1867, *Macewen* 1912 *Bergmann* 1931 *Compere & Adams* 1937, *Arkin & Katz* 1956 *Geiser* 1957, *Geiser & Trueta* 1958 *Ring* 1961, *Sunden* 1967) exist concerning the reaction of the longitudinal skeletal growth to nonloading or immobilization that have produced very varying results according to some growth stimulation according to others retardation The above thus argues against deliberately fracturing as a suitable method

The same objection can be raised against performing osteotomies Here also appears considerable trauma of soft parts whose possible influence however could be eliminated by sham operations

Drilling of the cortex could be said to represent a suitable form of trauma, at the same time as the experimental animal could be expected to load its damaged leg fairly normally According to *Hansson* (1967) periosteal lesion alone of the size required here produces very slight growth reaction, whereas drilling restricted to the cortex as well as drilling through the cortex across the medullary cavity could be expected to produce more pronounced growth stimulation The latter type of lesion could relatively well be compared to a fracture which in both diaphysis and metaphyses must usually result in destruction of medullary vessels It

should not be difficult to drill in the exact place and in the matter of the medullary cavity it seemed to be technically simple to allow the drill to pass across it and be stopped by the opposite cortex

It thus seemed most suitable to choose drilling combined with medullary trauma

Ad 2) The clinical investigation was made on humerus It was therefore logical to carry out the experimental study on this bone Humerus in rabbit however is not particularly suitable for growth determination with the tetracycline method because the proximal growth plate on axial sections is visualized as wavy or corrugated (*Hansson* personal communication) This was judged disadvantageous for the exactness of the planned measurements humerus was therefore rejected as experimental object

Tibia (tibio-fibula) is the long bone in rabbit that is most often used at different kinds of experimental studies It is easily accessible anatomically is large enough to allow various kinds of operations and its two growth regions offer no special problems at preparing

Another long bone whose qualities from experimental orthopaedic aspect can be considered favourable is radius This bone is also easily accessible and its growth regions are easy to prepare Moreover ulna is able to bear the body weight and the extremity is thus not out of function after an operation on radius

For these various reasons the author decided to use tibia and radius for his studies

In the matter of placing the drill traumata the intention was to try to reproduce the three clinical fracture variants in humerus by drilling holes in both tibia and radius either proximally metaphyseally diaphyseally or distally metaphyseally Concerning the metaphyseal drillings it was important not to produce lesion of the growth cartilage it was therefore decided regarding tibia to place the drill centre about 5 mm from the nearest part of the growth plate The drill was 2 3 mm diameter In the case of radius it was necessary to use a thinner drill diameter 1 6 mm otherwise the trauma could destroy almost the whole of the bone s bulk The diaphyseal drilling was made in both radius and tibia in the middle of the bone

Ad 3) There were no particular doubts concerning the measuring method The author s original purpose was to carry out determinations of the longitudinal growth by tetracycline labelling which when the study was to begin was used by *Hansson* (1964 1967) with success and compared with earlier measuring methods with an exactness never before attained

B The tetracycline labelling method for the determination of the growth rate of long bones

After *Andre s* (1956) discovery and *Milch et al s* (1957) more intensive study of the affinity of the tetracyclines to tissues during mineralization the various tetracyclines and perhaps especially oxytetracycline (OTC) have come into general use at the study of endochondral growth, lamellar bone formation, dentine and enamel formation (see, e g, *Hulth & Olerud* 1962, *Urist & Ibsen* 1963, *Hansson* 1964, 1967, *Sunden* 1967, *Ahlgren* 1968, *Persson* 1968)

Although OTC is undoubtedly toxic, this can be ignored in the doses required for intravital labelling of bone (*Hansson* 1967), and investigations made so far seem to show that this substance is the least harmful in the tetracycline group (*Harris et al* 1962, *Owen* 1963 1965, *Krenitz* (1965)

In agreement with *Hansson s* study of the OTC effect on the endochondral growth (1967) a dose of 1 0 mg/kg body weight was chosen This was administered intravenously in a marginal ear vein No signs of toxic effect in the form of deformed cartilaginous trabeculae in the growth region were observed with certainty at this dose The OTC preparation employed was Terramycin® *ad us vet* (Pfizer)

Hansson's method (1964 1967) was used for the preparing Thus the bones after being dissected out were fixed in absolute ethyl alcohol for 24—72 hours usually and preferably for 48 hours Longitudinal sections were then cut in the frontal plane with a razor blade while observing parallelity with the metaphyseal bone trabeculae The sections were placed for about 5 minutes in xylol and thereafter mounted in DePeX (Gurr London) The preparations were kept for 24 hours in a darkened room whereafter examination was made with fluorescence microscope

The optic equipment consisted of a binoculary *Zeiss* fluorescence microscope with a mercury lamp as source of light (Osram HBO 200 W) and a combination of primary filters BG 12/4 and BG 38/2 5, as well as barrier filter 47 A dark field condensor NA 0 65/0 85 was also used A measuring ocular (Kpl 12 5 x) furnished with a 10 mm micrometer with 100 divisions was used, as well as a plane achromatic objective 10 x (NA 0 22) The system was calibrated with the aid of an objective micrometer (Reichert) so that every division on the scale corresponded to 10 microns

C The timing of the investigation

Preliminary investigations showed that it was most suitable to carry out a 3 twenty four hour study of the growth where the skeletal trauma would be applied at the beginning of the second 24 hour period and where OTC would be administered 4 times at the beginning of the first second and third 24 hour period and at the end of the third immediately before the animal was sacrificed Thus four fluorescing OTC injection zones would be obtained (for measuring points see below) These are designated A B C and D in the following

Distance A—B	growth increase during the pre operative 24 hour period = normal growth
Distance B—C	growth increase during the first postoperative 24 hour period
Distance C—D	growth increase during the second postoperative 24 hour period



Fig 18 Microphotograph of proximal tibial metaphysis from growing rabbit with the four fluorescing oxytetracycline zones mentioned on p

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Hansson's method (1964, 1967) was used for the preparing. Thus the bones after being dissected out were fixed in absolute ethyl alcohol for 24—72 hours, usually and preferably for 48 hours. Longitudinal sections were then cut in the frontal plane with a razor blade, while observing parallelity with the metaphyseal bone trabeculae. The sections were placed for about 5 minutes in xylol and thereafter mounted in DePeX (Gurr, London). The preparations were kept for 24 hours in a darkened room whereafter examination was made with fluorescence microscope.

The optic equipment consisted of a binocular *Zeiss* fluorescence microscope, with a mercury lamp as source of light (Osram HBO 200 W) and a combination of primary filters BG 12/4 and BG 38/2.5 as well as barrier filter 47. A dark field condensor NA 0.65–0.85 was also used. A measuring ocular (Kpl 12.5 x) furnished with a 10 mm micrometer with 100 divisions was used, as well as a plane achromatic objective 10 x (NA 0.22). The system was calibrated with the aid of an objective micrometer (Reichert) so that every division on the scale corresponded to 10 microns.

C The timing of the investigation

Preliminary investigations showed that it was most suitable to carry out a 3 twentyfour hour study of the growth where the skeletal trauma would be applied at the beginning of the second 24 hour period and where OTC would be administered 4 times at the beginning of the first second and third 24 hour period and at the end of the third immediately before the animal was sacrificed Thus four fluorescing OTC injection zones would be obtained (for measuring points see below) These are designated A B C and D in the following

Distance A—B	growth increase during the pre operative 24 hour period =normal growth
Distance B—C	growth increase during the first postoperative 24 hour period
Distance C—D	growth increase during the second postoperative 24 hour period



Fig 18 Microphotograph of proximal tibial metaphysis from growing rabbit with the four fluorescing oxytetracycline zones mentioned on p

B The tetracycline labelling method for the determination of the growth rate of long bones

After *Andre s* (1956) discovery and *Milch et al's* (1957) more intensive study of the affinity of the tetracyclines to tissues during mineralization the various tetracyclines and perhaps especially *oxytetracycline* (OTC) have come into general use at the study of endochondral growth lamellar bone formation dentine and enamel formation (see, e g *Hulth & Olerud* 1962 *Urist & Ibsen* 1963, *Hansson* 1964, 1967 *Sunden* 1967, *Ahlgren* 1968 *Persson* 1968)

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D Operation method

As described on p 72 the author chose to carry out proximal mid diaphyseal and distal drillings of tibia and radius (cf Fig 19 and 20)

The number of animals in each of the six categories is listed in the following table

Tibia proximal drilling	69
mid diaphyseal drilling	54
distal drilling	70
Radius proximal drilling	63
drilling	39
distal drilling	75
Sham operation tibia	6
radius	6
Narcosis alone	15
No measure (control of normal growth) tibia	3
No measure (control of normal growth) radius	4
	404

The procedure at operation was as follows

Evipan i v supplemented with ether was used as anaesthetic After the animal had been anaesthetized the extremity was shaved to the required extent A longitudinal incision was made through skin and fascia 12—15 mm long The musculature was bluntly parted In the periosteum a door shaped flap about 5×5 mm was cut and folded upwards taking care that it did not reach the level of the growth plate during loosening Centrally in the periosteal opening a hole was made with a dental drill at right angles to the longitudinal axis of the bone In the case of the metaphyseal drillings it was relatively easy to distinguish the growth plate and to place the drill hole at the intended distance from it Regarding tibia the drill hole was throughout placed tibially in radius dorsally Left leg was operated on consistently

Thus, after the experimental animals had arrived, been weighed and observed for about 3 days, a first OTC-injection (section zone A) was made *24 hours later, with a maximum margin of error of ±5 minutes* (according to *Hansson's* normal growth curves 1967, corresponding to a growth of approximately ±2 microns), a new weighing a new OTC injection (zone B), *and immediately thereafter drilling were made 24 hours* after B, weighing and injection (zone C) followed 24 hours after C weighing and injection (zone D) were repeated The animal was then killed The preparing was carried out according to the previously given principles Sections, usually 3 from each growth region, were taken from the proximal and *distal growth regions bilaterally, thus from both the* operation side and the control side, in radius or tibia, according to where the operation was performed

In the sections from each of these 4 growth regions 5 measurements (distributed, if possible, on the 3 sections) were then made of the distance A—B 5 of B—C, and 5 of C—D Thus from each experimental animal 60 measurements were obtained However quite often, for various reasons it was not possible to get 5 measurements from each growth region for the 24-hour growth If fewer than 3 measurements were obtained, this 24 hour value was discarded as was the corresponding measurement for the contra lateral growth region for the same 24-hour period

For *uniformity of judgement* the author carried out all measurements The metaphyseal front of each OTC-band was chosen as measuring point (according to *Hansson* 1967)

After a number of 3 twenty four hour period recordings of this typ were obtained, it was decided to study the course of the growth over a longer time from the trauma According to the same schedule as above and maintaining the *24* hour *interval* between the OTC injections *a series of* data were collected for different 3 twenty four hour periods from the time of the operation up to the tenth postoperative 24 hour period as evenly distributed as possible

The day after the operation the animals fed and moved normally, as far as could be judged Infection of the operation wounds was noted on only three occasions and these animals were rejected from the series

Besides these six different drillings a few sham operations were carried out 6 on tibia and 6 on radius This was to discover any possible growth disturbing effect from merely skin and muscle incisions For similar purposes 15 animals given only narcosis were investigated These last mentioned investigations followed the original time schedule (pre operative 24 hours + 2 postoperative 24 hours)

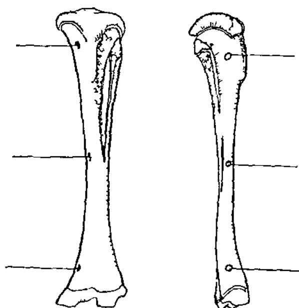


Fig 19 Front and side of tibiofibula in rabbit The position of the three drillings is indicated

The drilling was done in stages to avoid the generation of heat As soon as the medullary cavity was reached, rotation was stopped and the now stationary drill was pushed in towards the opposite wall When the cavity was penetrated, there was usually moderate bleeding at proximal and diaphyseal tibial drilling otherwise none The bleeding, however usually ceased when the wound was sutured (silk) and no postoperative haematoma worth mentioning was noted The wounds were not bandaged

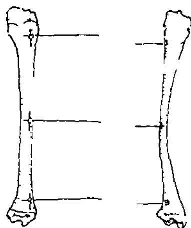


Fig 20 Front and side of radius in rabbit The position of the three drillings is indicated

The day after the operation the animals fed and moved normally, as far as could be judged Infection of the operation wounds was noted on only three occasions and these animals were rejected from the series

Besides these six different drillings a few sham operations were carried out 6 on tibia and 6 on radius This was to discover any possible growth disturbing effect from merely skin and muscle incisions For similar purposes 15 animals given only narcosis were investigated These last mentioned investigations followed the original time schedule (pre operative 24 hours + 2 postoperative 24 hours)

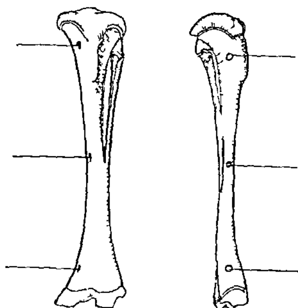


Fig 19 Front and side of tibiofibula in rabbit The position of the three drillings is indicated

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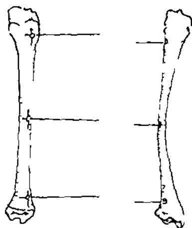


Fig 20 Front and side of radius in rabbit The position of the three drillings is indicated

CHAPTER IX

RESULTS

A Remarks on sources of error

Although growth determination with oxytetracycline labelling can in the main be said to be a relatively simple method some difficulties arose at the investigation As elaborated in more detail by *Hansson* (1967) the *fluorescing* zones become successively weaker during their seeming progress in diaphyseal direction which of course is due to the movement of the growth plate in epiphyseal direction This applies to both tibia and radius to about the same extent The last three injections as a rule resulted in quite *distinct lines* in the preparation There was no difficulty in measuring between these zones The first injection administered 72 hours *before killing* the animal on the other hand was frequently weak and diffuse *therefore* measurement of the interval between the OTC lines A and B (cf p 000) could not be carried out on every occasion

The postoperative development of a tongue of cartilaginous cells from the growth plate down in the metaphysis (cf *Hansson* 1967) could sometimes *considerably* restrict the space for transversally running fluorescing bands thereby reducing the possibility of repeated measurements in one and the same section

The growth potential of the proximal growth plate in radius is only about 20 % of that in the distal radius and in the two ends of tibia The intervals (i e the daily growth) measured in the proximal radius metaphysis were 80—130 μ wide and the measuring *scale was* graded in 10 μ units It is then easily understood that the percentage *error* in measurement must have been *considerably* greater in the proximal radius than in the other three growth regions studied here with a daily growth of 400—500 μ (cf *below*)

Of error factors otherwise the toxic effect of OTC already mentioned does not appear to have played any role An incorrect orientation of the cuttings could result in considerable distortion of the measuring intervals but such a faulty oblique cutting is fairly clearly reflected in the appearance of the trabeculae in the preparation

E Additional statistical methods

The statistical analysis of the experimental study results have in the main followed the same line as given on pp 000 As statistical working model, the following differences were used

$$d_{ij} = X_{Fij} - X_{Cij} \quad \text{where} \quad \begin{matrix} i = 1, 2, 3 \quad\quad n \text{ (animals)} \\ j = 1, 2, 3 \quad\quad \text{(24 hour-periods)} \end{matrix}$$

X_{Fij} is the measurement value for the fractured bone of the i^{th} animal after the j^{th} day

X_{Cij} is the measurement value for the control bone of the i^{th} animal after the j^{th} day

The same model was arranged for the three different drilling places in combination with two bone types (radius, tibia) and two measurement places

This model was chosen in order that any possible weight effect could be eliminated by using the differences because the weight effect must be considered to be equally great for fractured bone and control bone

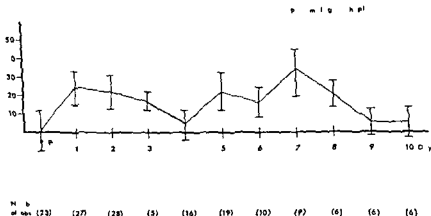
The analysis was made with the aid of one sided variance analysis (t-analysis) whereby the interest was primarily concentrated on possible differences between the 24 hour periods (*Snedecor* 1962, *Guenther 1964*)

B Effect of drilling on growth rate

1 Operated bone

Tibia (proximal drilling) Fig 21 22 Table 6

Proximal growth plate the growth rate shows an almost significant acceleration for the first second and third postoperative 24 hour periods whereafter there is a fall to statistically not guaranteed differences up to and including the sixth 24 hour period The seventh and eighth 24 hour periods again show an almo t significant acceleration whereafter the growth during the ninth and tenth 24 hour periods approaches more and more that of the control bone



F g 21

P oximal d ll n of tibia
Ave age da ly n ease in g owth from the proximal growth plate

Distal growth plate the reaction of the distal epiphysis is highly significant and reaches a maximum during the third to fifth postoperative 24 hour periods although almost significant acceleration can be observed as early as the first 24 hour period after the drilling Also concerning the distal epiphysis there is a tendency to a second maximum at the seventh 24 hour period, but the number of observations here are relatively few and the significance uncertain It is conspicuous that the reaction from the distal

The existence of a litter effect, a product of hereditary and environmental factors and shown by *Hansson* (1967) to have a significant influence on the rate of growth, was counteracted by animals from one and the same litter always being split up on various types of drillings and one type of drilling always being performed on animals from at least three different litters

The total systematic error of method at a single measurement has been calculated statistically (col A below) However, the values used for growth calculations were arithmetic means based on 5 measurements and the error of method for these values (col B) was consequently reduced by a

$$\text{factor} = \frac{1}{\sqrt{5}}$$

	A	B	B expressed in % of average daily growth
Tibia proximal growth plate	17 3μ	7 7μ	1 4
Tibia distal growth plate	14 4μ	6 4μ	1 5
Radius proximal growth plate	8 1μ	3 6μ	2 8
Radius distal growth plate	10 5μ	4 7μ	1 1

The growth thus recorded is the diaphyseal growth As pointed out on p 000 this does not correspond exactly to the growth recorded in *Part One*, where also the growth of the bony epiphysis is included According to *Hansson* (1964), however the epiphyseal proportion of the total growth of the bone in rabbit at this age period is less than 1/5 of the diaphyseal and it was deemed possible to disregard this fraction in the following discussions of the experimental and clinical results

B Effect of drilling on growth rate

1 Operated bone

Tibia (proximal drilling) Fig 21 22 Table 6

Proximal growth plate the growth rate shows an almost significant acceleration for the first second and third postoperative 24 hour periods whereafter there is a fall to statistically not guaranteed differences up to and including the sixth 24 hour period The seventh and eighth 24 hour periods again show an almost significant acceleration whereafter the growth during the ninth and tenth 24 hour periods approaches more and more that of the control bone

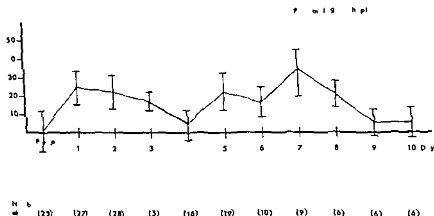


Fig 21

P oximal d ll ng of t bia
Ave age d ly nc ease in growth from the p oximal growth plate

Distal growth plate the reaction of the distal epiphysis is highly significant and reaches a maximum during the third to fifth po toperative 24 hour periods although almost significant acceleration can be observed as early as the first 24 hour period after the drilling Also concerning the distal epiphysis there is a tendency to a second maximum at the seventh 24 hour period but the number of observations here are relatively few and the significance uncertain It is conspicuous that the reaction from the distal

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The total systematic error of method at a single measurement has been calculated statistically (col. A below). However, the values used for growth calculations were arithmetic means based on 5 measurements, and the error of method for these values (col. B) was consequently reduced by a

$$\text{factor} = \frac{1}{\sqrt{5}}$$

	A	B	B expressed in % of average daily growth
Tibia proximal growth plate	17.3 μ	7.7 μ	1.4
Tibia distal growth plate	14.4 μ	6.4 μ	1.5
Radius proximal growth plate	8.1 μ	3.6 μ	2.8
Radius distal growth plate	10.5 μ	4.7 μ	1.1

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B Effect of drilling on growth rate

1 Operated bone

Tibia (proximal drilling) Fig 21 22 Table 6

Proximal growth plate the growth rate shows an almost significant acceleration for the first second and third postoperative 24 hour periods whereafter there is a fall to statistically not guaranteed differences up to and including the sixth 24 hour period The seventh and eighth 24 hour periods again show an almost significant acceleration whereafter the growth during the ninth and tenth 24 hour periods approaches more and more that of the control bone

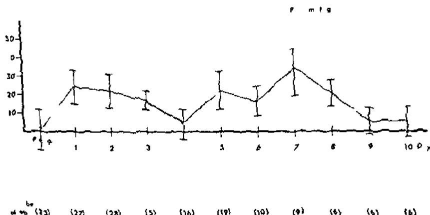


Fig 21

Proximal drilling of tibia
Average daily increase in growth from the proximal growth plate

Distal growth plate the reaction of the distal epiphysis is highly significant and reaches a maximum during the third to fifth postoperative 24 hour periods although almost significant acceleration can be observed as early as the first 24 hour period after the drilling Also concerning the distal epiphysis there is a tendency to a second maximum at the seventh 24 hour period but the number of observations here are relatively few and the significance uncertain It is conspicuous that the reaction from the distal

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seventh partly highly significant values with a probable maximum during the third to sixth 60 μ No tendency to a second maximum appears

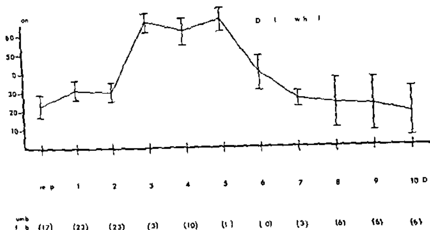
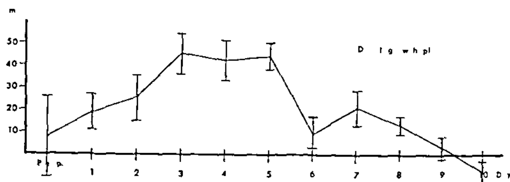


Fig 24
Mid diaphyseal drilling of tibia
Average daily increase in growth from the distal growth plate

Distal growth plate Here a strong reaction is recorded with highly significant values during the first and second postoperative days where after the overgrowth becomes even more intense and reaches a maximum during the third to the fifth 24 hour periods where the absolute values are 60 to 65 μ From and including the sixth period a regress occurs and from and including the eighth no statistically guaranteed difference compared with the control bone can be recorded

In this series a strange incongruity appears the growth already shows a significant increase pre operatively compared with the control bone Careful examination of the preparations and the records of the experimental animals gave no explanation for this phenomenon which however is not absurd from a statistical standpoint Probably its occurrence suggests that the recorded growth acceleration during the postoperative first and second 24 hour periods must be granted limited statistical significance



Numb f bs. (19) (26) (27) (10) (15) (21) (12) (9) (6) (6) (6)

Fig 22
Proximal drilling of tibia
Average daily increase in growth from the distal growth plate

growth plate is considerably stronger in that its maximum lies at 45 μ whereas the maximum point for the proximal growth plate during the first 24-hour period is 25 μ and during the seventh (more uncertain) 35 μ

Tibia (mid diaphyseal drilling) Fig 23 24 Table 7
Proximal growth plate the growth shows almost significant increase already during the first postoperative 24 hour period and during the third to

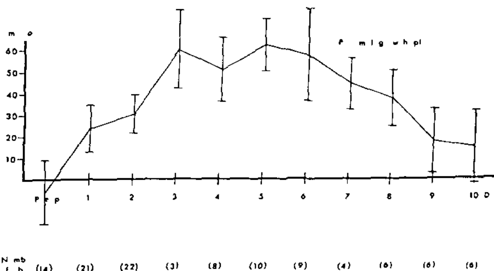


Fig 23
Mid diaphyseal drilling of tibia
Average daily increase in growth from the proximal growth plate

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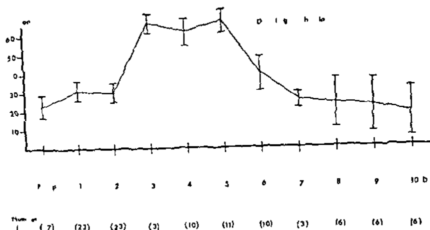


Fig 24
Mid diaphyseal drilling of tibia
Ave age daily inc ease in g owth f om the d stal growth plate

Distal growth plate Here a strong reaction is recorded with highly significant values during the first and second postoperative days where after the overgrowth becomes even more intense and reaches a maximum during the third to the fifth 24 hour periods where the absolute values are 60 to 65 μ From and including the sixth period a regress occurs and from and including the eighth no statistically guaranteed difference compared with the control bone can be recorded

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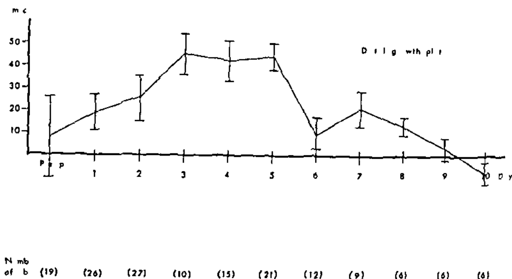


Fig 22
Proximal drilling of tibia
Average daily increase in growth from the distal growth plate

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Tibia (mid diaphyseal drilling) Fig 23, 24 Table 7

Proximal growth plate the growth shows almost significant increase already during the first postoperative 24 hour period, and during the third to

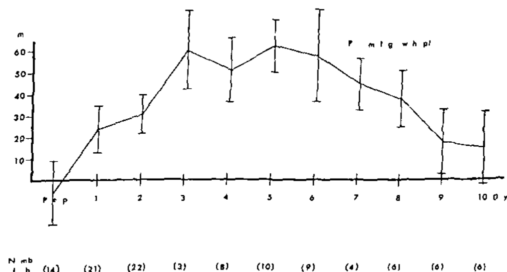


Fig 23
Mid diaphyseal drilling of tibia
Average daily increase in growth from the proximal growth plate

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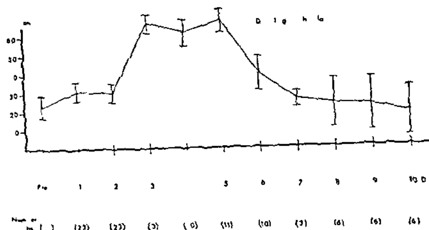


Fig 24
Mid-diaphyseal drilling of tib a
Ave ge daily increase in growth f om the distal g owth plate

Distal growth plate Here a strong reaction is recorded with highly significant values during the first and second postoperative days where *after the* overgrowth becomes even more intense and reaches a *maximum* during the third to the fifth 24 hour periods where the absolute values are 60 *to* 65 μ From and including the sixth period a *regress occurs* and from and including the eighth no statistically *guaranteed difference compared* with the control bone can be recorded

In this series a strange incongruity appears the growth already shows a significant increase pre-operatively compared *with the control* bone Careful examination of the preparations and *the records* of the experimental animals gave no explanation for *this* phenomenon which however is not absurd from a statistical standpoint. *Probably* its occurrence suggests that the recorded growth *accelera on during* the postoperative first and second 24 hour periods must be granted limited statistical *significance*

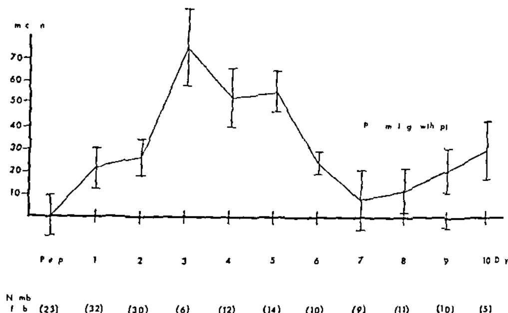


Fig 25
Distal drilling of tibia
Average daily increase in growth from the proximal growth plate

Tibia (distal drilling) Fig 25, 26 Table 8

Proxim1l growth plate The first postoperative 24-hour period shows an almost significant growth increase, which has full significance the following *5 days and where a maximum is judged to be present during the third to* fifth 24 hour periods The 1bsolute value of this maximum probabl} does *not exceed 60 μ*, because the extremel} high peak *(74 μ)* in the third period

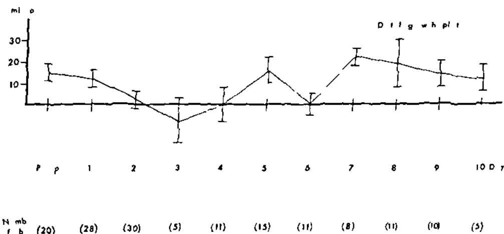


Fig 26
Distal drilling of tibia
Average daily increase in growth from the distal growth plate

is based on rather few measuring values From and including the seventh 24 hour period the growth has slowed down to that of the control bone without reliable signs of any second maximum

Distal growth plate Inconclusive reaction with some tendencies to both growth acceleration and retardation A significant overgrowth value for the seventh 24 hour period is based on comparatively few observations Besides there is a tendency although less pronounced to the same discrepancy between the preoperative growth of the two bones as noted in the series of mid diaphyseal drillings

Radius (proximal drilling) Fig 27 28 Table 9

Proximal growth plate The difference in growth rate during the preoperative 24 hours compared with the control bone has no statistical significance In agreement with the slight growth potential of the proximal growth plate the reactions on the whole are small and statistically guaranteed acceleration is observed only during the first postoperative 24 hour period whereas the fluctuations of the curve otherwise lack significance

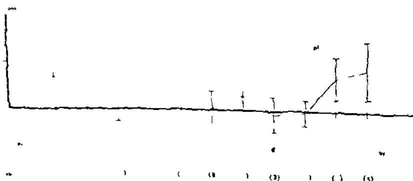


Fig 27
Proximal drilling of radius
Averaged daily increase in growth from the proximal growth plate

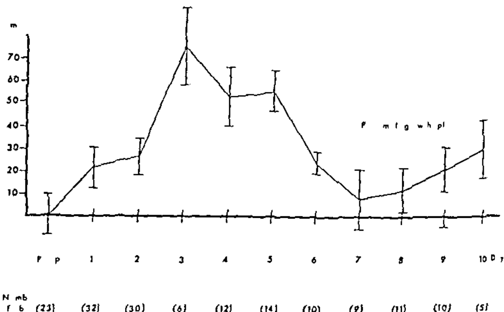


Fig 25
Distal drilling of tibia
Average daily increase in growth from the proximal growth plate

Tibia (distal drilling) Fig 25, 26 Table 8

Proximal growth plate The first postoperative 24 hour period shows an almost significant growth increase, which has full significance the following 5 days and where *a maximum is judged to be present during the third to* fifth 24-hour periods The absolute value of this maximum probably does not exceed 60 μ, because the extremely high peak (74 μ) in the third period

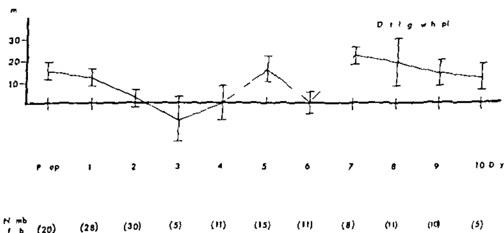


Fig 26
Distal drilling of tibia
Average daily increase in growth from the distal growth plate

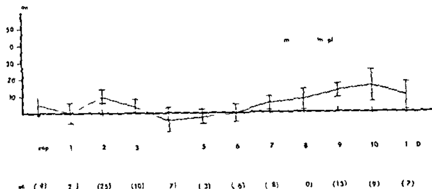
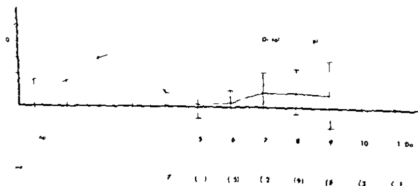


Fig 29
D stal drilling of radius
Average daily increase in growth from the proximal growth plate

Radius (distal drilling) Fig 29 30 Table 11

Proximal growth plate as expected with regard to the slight growth potential of this region the response to the drilling was slight Almost significant reaction however is shown during the second postoperative 24 hour period otherwise the results have no statistical significance As at proximal drilling in tibia a slight tendency to two maxima can be discerned one at the second postoperative 24 hour period and one at the ninth to tenth but this observation is uncertain

Distal growth plate almost significant to highly significant reaction is obtained during the first to second postoperative 24 hour periods whereafter successive equalization takes place



F g 3
D tal d ill ng f ad
Ac age dai y nc ea e in g owth f om the d stal g owth plate

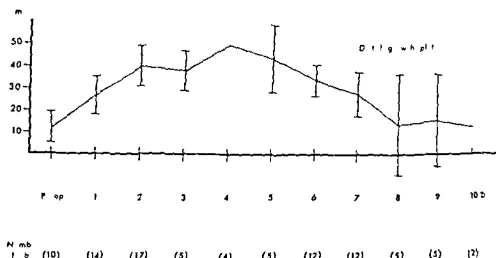


Fig 28
Proximal drilling of radius
Average daily increase in growth from the distal growth plate

Distal growth plate concerning the pre-operative 24 hour period the same condition applies as for the proximal growth plate A significant acceleration is found during the first postoperative 24-hour period, and a high significance during a maximum in the third to fifth periods whereafter a slow regress occurs The maximum value in the fourth 24 hour period appearing on the curve is based on only 4 observations and must be considered fairly uncertain The actual absolute maximum value probably lies lower around 45 μ

Radius (mid diaphyseal drilling) Table 10

Proximal growth plate the course of the curve above the x axis indicates only a slight and uncertain tendency to overgrowth without statistical significance for any 24-hour period Because of the absence of distinct positive or negative growth reaction diagrammatic representation has been omitted

Distal growth plate although the curve reaches relatively high peaks in the second and the fourth 24 hour periods the spreading in the observations is none the less large and the reaction has no statistical significance for any 24 hour period This investigation was considerably disturbed by a strong development of tongues of cartilaginous cells (cf p 000) the number of observations were therefore particularly few in this series Diagram omitted

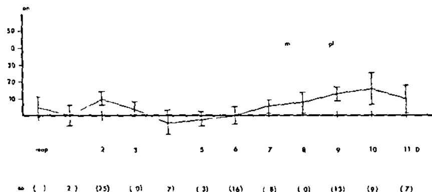


Fig 29
Distal drilling of radius
Average daily increase in growth from the proximal growth plate

Radius (distal drilling) Fig 29 30 Table 11

Proximal growth plate as expected with regard to the slight growth potential of this region the response to the drilling was slight Almost significant reaction however is shown during the second postoperative 24 hour period otherwise the results have no statistical significance As at proximal drilling in tibia a slight tendency to two maxima can be discerned one at the second postoperative 24 hour period and one at the ninth to tenth but this observation is uncertain

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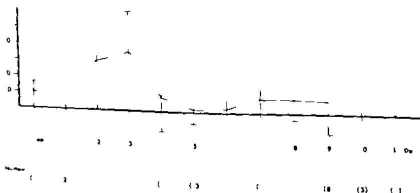


Fig 30
Distal drilling of radius
Average daily increase in growth from the distal growth plate

2 Control bone

In this investigation, the growth *of the control bone during the first* and second postoperative 24 hour periods was compared with the growth durin the *pre-operative* 24-hour period, with t analysis *In* agreement with *Hansson's* (1967) investigation, growth retardation can here be recorded in most instances The results were as follows (cf Table 12)

Proximal drilling of tibia

Proximal growth plate highly significant retardation during the first and second postoperative 24 hour periods Average retardation for 2 periods, 35 μ

Distal growth plate highly significant retardation during the first post operative period, almost significant the second Average retardation for 2 periods, 24 μ

Mid diaphyseal drilling of tibia

Proximal growth plate almost significant retardation during the first postoperative period no significance during the second Average retardation for 2 periods 16 μ

Distal growth plate no significant change in growth during any of the investigated periods Average retardation is 22 μ but the spreading is large

Distal drilling of tibia

Proximal growth plate highly significant growth retardation during the first and second postoperative periods Average retardation for a period 30 μ

Distal growth plate highly significant retardation during the first post *operative period significant during the second* Average retardation for 2 periods 26 μ

Proximal drilling of radius

Proximal growth plate no significant retardation during the first two post operative periods

Distal growth plate almost significant growth retardation during the first postoperative period Slight acceleration of 14 μ during the second but without significance (the only acceleration noted in the control bone during the period in question at any of the drillings)

Mid diaphyseal drilling of radius

Because of few usable complete 3 twentyfour hour series no statistical analysis was made on this material

Distal drilling of radius

Proximal growth plate almost significant retardation and this only during the first postoperative period

Distal growth plate significant retardation during the first postoperative period Non significant reaction during the second

C Control experiments

1 Sham operations

With the object of discovering whether skin incision and muscle incision up to, but not through, the periosteum can affect growth 12 rabbits were operated on in this manner 6 on the proximal radius, and 6 on the proximal tibia The investigation included the first three postoperative 24 hour periods Tetracycline labelling was done according to the same norms as for the other material For none of the studied periods, do any of the bones show statistically demonstrable difference concerning growth either for the proximal or for the distal growth regions The results are reported in table nr 13 (see Appendix)

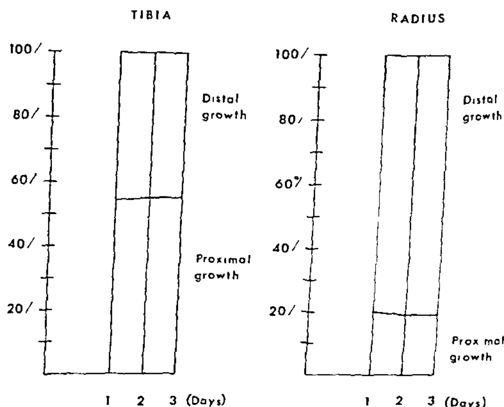


Fig 31 Growth percentage from proximal and distal growth plates in tibia and radius of the rabbit estimated from 15 non-operated animals

2 *Control rabbits (narcosis)*

An investigation was made concerning growth in 15 rabbits taken from different litters and given narcosis during the 24 hour period before and the two periods after the narcosis In agreement with earlier investigators (*Hansson 1967*) no statistically demonstrable differences whatever were obtained between the three periods in other words the narcosis had no effect These 15 animals were therefore regarded as normal material and on the basis of their growth the percentage size of the systematic error (P 82) was calculated By combining the values of the three periods the percentage growth from the proximal growth regions in tibia and in radius was also calculated whereby the following confidence intervals were obtained

Tibia	Radius
$P = (55\ 2 \pm 1\ 5)\ \%$	$P = (19\ 6 \pm 1\ 3)\ \%$

According to this investigation the proximal growth rate in rabbits of this age in tibia is thus 55 % and the distal 45 % whereas the corresponding values for radius is 20 % and 80 % respectively

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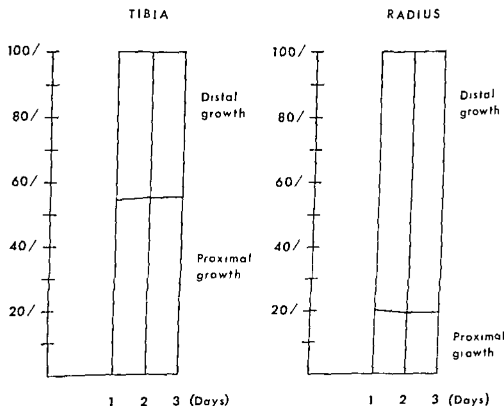


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CHAPTER X

DISCUSSION

The experimental operations on tibia — reported in previous chapters — seem to have so pronounced and unambiguous effect that an error factor would have to be very considerable to produce faulty results The same applies to proximal drilling of radius whereas drilling centrally or in the distal metaphysis of the same bone gave uncertain values The statistical analysis method has eliminated possible weight factor The sex of the animals at the age of 30—40 days has no influence on the growth rate (*Hansson* 1967) The systematic errors for a single measurement in proximal and in distal tibia is indicated on p 82 as 17 3 and 14 4 μ respectively (i e about the same size as that given by *Hansson* 1967) and does not affect the statistical evidence The results from distal radius can be appraised according to the same norms The values from the proximal growth region of radius are lower which might be largely due to the slight growth rate from its growth plate Here the absolute value of the systematic error is actually lower 8 1 μ this, however with regard to the low growth rate is in per cent an error of method fully twice as large as in other investigated growth regions

As earlier mentioned (p 63) the object of the experimental investigation was to find out whether a varying localization of fractures in a growing long bone gave different growth stimuli It was therefore natural to study in more detail the reaction from the proximal and the distal growth regions in a long bone after an experimental trauma For this reason the discussion here is restricted to the relation between trauma localization and increased growth from the two growth plates of a long bone

At a study of Fig 21 and 22 (proximal tibia drilling) and Fig 25 and 26 (distal tibia drilling) it is obvious that the growth plate lying farthest from the trauma shows the strongest reaction which is most evident after distal drilling This is verified by the statistical calculation

A comparison with the post traumatic reaction from the growth plates of radius reveals that the relation is similar in this bone concerning proximal drilling whereas distal trauma gave no significant differences This is

D Summary of the results

Operated bone	Position of the drill trauma	Growth reaction Proximally	Distally
Tibia	proximal	+	+++
	mid diaphyseal	+++	+++
	distal	+++	+(+)
Radius	proximal	+(+)	+++
	mid-diaphyseal	0	0
	distal	+	+++

The grading in the above table follows the statistical evaluation Thus 0 does not indicate total absence of all reaction but only that statistical significance for such is lacking

both instances important for the growth process in adjoining growth region *Hansson* (1967) as mentioned earlier, demonstrated that where the trauma is extra medullary and restricted to a limited area of the cortical bone tissue or periosteum a growth stimulus is obtained both in the proximal and in the distal growth region of the same long bone it is therefore of importance whether or not the circulation paths of the growth region are intact

This investigation similar to earlier growth studies (*Brodin* 1955, *Elo* 1960 *Hansson* 1967) thus strongly argues against the opinion held by *Trueta* (1953 1958) *Taillard & Morscher* (1965) *Yabsley & Harris* (1965) These have asserted that a medullary trauma like extensive periosteal stripping stimulates the growth from the adjoining growth region by increasing the blood flow through the remaining blood vessels Results submitted here indicate on the other hand that a fracture equivalent trauma to long bones results in considerable vascular destruction in adjoining growth region which cannot be overcompensated by hyperaemia so that the growth here is unable to increase (and possibly be temporarily retarded, cf *Hansson* 1967) whereas an obvious growth stimulus appears early within the more distant growth plate

There is much that argues for growth stimulus being related to hyperaemia in the growth region involved This is also supported by investigations of *Wray et al* (1960 1961) and *Sunden* (1967) who found a positive correlation between blood flow and growth rate as well as *Persson* (1968) who found a positive correlation between oxygen tension and growth rate In accordance with this after a metaphyseal trauma such as those under discussion hyperaemia should be expected mainly within the remoter growth region and not or at least to a much lesser degree around the nearest growth plate This presumption might be checked further by several experimental methods

The diaphyseal drillings in tibia produced clearly significant and approximately equally strong reactions from both growth plates The increase in length of the long bone resulting from the experiments was therefore probably most considerable at mid diaphyseal drilling of tibia This result might be explained by the loss of the blood supply through the nutrient vessels caused by the drill trauma being probably thoroughly compensated by remaining vessels to the growth regions

With regard to the fact that *Hansson* (1967) noted changed growth rate (retardation) in the control bone after trauma to tibia the present author s statistical analysis also included an investigation of whether the control bone is affected by drilling in the contralateral bone In good agreement with *Hansson* s observations obvious retardation was obtained from the

easily understandable because the growth rate in the proximal growth region of radius is low compared with other studied regions It must be pointed out at the same time that the systematic error for this growth plate is greater than for the other three because of its small size and the thereby created sectioning difficulties On the basis of these observations in radius and tibia, it seems reasonable to conclude that metaphyseal drilling or *fracture in growing long bone is followed by strong growth stimulus from* the growth plate at the opposite end of the bone and slight (or no) acceleration from that lying nearest Earlier experimental investigations support *this concept Thus Brodin (1955) could demonstrate that periosteal stripping* in the proximal part of the tibia diaphysis in rabbit is regularly followed by a growth increase from the distal growth plate, and after a shorter *initial acceleration by a slowing down of the growth from the proximal* growth plate *Brodin* assumed that the lesion of proximal perforating metaphyseal *vessels caused, to some extent at least, the proximal growth* retardation

Reidy Lingley, Gall & Barr (1947) studied the effect of rontgen radiation on skeletal growth and could regularly demonstrate retarded growth from irradiated proximal epiphyseal region of the tibia and accelerated growth from the untreated distal growth zone of the same bone The authors suggested hyperaemia as a possible cause of this distal reaction

A distinct and fully significant reaction from the distal growth plate was obtained by *Hansson* (1967) after plugging of the medullary cavity in the proximal part of the tibia in rabbit The proximal growth plate showed initially a slight growth acceleration which was *followed by a* prolonged retardation of the *growth rate*

The results from the author s investigation thus agree well with those from the above mentioned studies The present investigation, moreover *clearly revealed that a trauma of the distal metaphysis* in tibia produces pronounced growth stimulus in the proximal growth region of the same long bone whereas the effect distally has much less significance A corresponding reaction pattern was also demonstrated in radius, whose largest growth occurs from its distal growth region as distinct from the condition in tibia Thus the reaction pattern is the same irrespective of whether it refers to the upper or lower extremity or whether the most rapidly growing growth region is situated proximally *or* distally

It must be pointed out however that this probably applies only if the trauma affected and destroyed the medullary vessels (fracture osteotomy, medullary *cavity drilling or plugging) and/or sufficient number of the* perforating metaphyseal blood vessels (periosteal stripping) which are in

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Summing up the principal results it can thus be said

that proximal drill trauma through the medullary cavity in growing rabbit tibia results in powerful increase in growth distally

that distal drill trauma in the same long bone gives a powerful increase in growth proximally and

that several criteria argue for such a growth reaction being a general phenomenon

two growth plates of the control bone after most types of drillings This reaction appears to be most powerful in the growth regions that have the highest growth potential in each bone the proximal growth plate in tibia and the distal growth plate in radius

It seems remarkable that mid diaphysary tibia drilling, which triggers off the most powerful total growth acceleration in the operated bone, also produces a very weak retardation in the control bone This may however be ascribed to the anatomical conditions in the mid diaphyseal region being such that an exposure of the shaft is easy and less traumatic to the soft parts than a dissection of the metaphyses In other words, the general debilitating effect of the experimental operations is probably slightest at drillings of the tibia diaphysis

Repeated allusions (p 87, 96) have been made to a supposition that over growth probably is more pronounced in growth regions with a high growth potential This may be a reasonable assumption but has no factual foundation *Some viewpoints on this question can be extracted from the present* material

In rabbit tibia the proportions of growth from proximal and distal growth plates are found to be 55 % and 45 % respectively (p 93) For such a slight difference to be mirrored with certainty in the recordings of overgrowth a very large material is required At a comparison between the diagrams for proximal growth plate reaction on distal drilling (Fig 25) and distal growth plate reaction on proximal drilling (Fig 22) a certain difference can no doubt be perceived where the proximal growth plate shows the strongest reaction (maximum 60 μ in contrast to 45 μ for the distal growth plate) However, statistical significance cannot be ascribed to this difference

If we look at the corresponding values within radius (Fig 29 28) where proximal and distal growth contributions are 20 % and 80 % respectively, a clear difference is observed with a maximum for the proximal plate at 10 μ and for the distal at about 40 μ That the proportions for radius happen to fit exactly should be regarded as a chance coincidence but even with appropriate criticism some evidence must be considered to exist for the supposition that the amount of overgrowth is correlated to the natural growth potential of the region in question

It should also be mentioned here that the experimental results refer to the initial reaction whereas the clinical results refer to the growth reaction 3 months or more after the fracture when the healing had reached an advanced stage Moreover at the clinical investigation the change was recorded in the total length of the long bone — diaphysis cartilage plates and bony epiphyses — whereas solely the growth of the diaphysis was measured in the different growth plates of the long bone at the experimental investigation.

The experimental trauma that resulted in the strongest total increase in length was drilling in the centre of the tibia diaphysis whereby both proximal and distal growth plates reacted with high significance and large absolute measuring values If analogous conditions exist concerning humerus in *homo* it could be expected that the diaphysary humerus fractures would give the strongest increase in growth as suggested by *Calati & Poli* 1959 This is not so in the present material where the dislocated diaphysis fractures show accumulated overgrowth of 7 mm compared with 9 mm for *collum chirurgicum* fractures and 9 mm for dislocated supracondylar fractures

Also here there is the reservation of course that the experimental and the clinical investigations from physiological aspect do not take place in the same period The *foramen nutritium* in humerus in *homo* moreover is situated somewhat below the most often observed level for diaphyseal fractures whereas *foramen nutritium* in rabbit tibia lies on about the same level as the point where the diaphysary drill holes are made It is therefore conceivable that a diaphysis fracture in humerus in *homo* is sometimes more likely to correspond to the proximal drill trauma in rabbit tibia than to the trauma to the centre of the tibia diaphysis In cases of this nature it can be expected that humerus fractures in diaphysis and within *collum chirurgicum* must trigger off growth acceleration of about the same size This occurred in the present material but the number of observations is not large enough to confirm with any certainty the above reasoning

CONCLUDING REMARKS ON THE CLINICAL APPLICATION OF THE EXPERIMENTAL RESULTS

As pointed out in the introduction the growth rate in humerus in *homo* differs considerably in the proximal and distal growth plates the relation being given as 3 1 by a couple of investigators (*Bergmann* 1928—29, *Emneus & Hedstrom* 1964) If the experimental results are universal for the effects of fractures on the growth regions of long bones, it could be expected that a supracondylar humerus fracture would stimulate the proximal growth plate and that a fracture through *collum chirurgicum* would, in the main, influence the distal growth zone With reference to the mentioned relation between the growth rates, a supracondylar fracture should produce considerably greater growth stimulus than a *collum chirurgicum* fracture comparable regarding dislocation and age of the individual

As seen in Chapter IV, the accumulated average growth concerning fractures through *collum chirurgicum* was in the present material 9 mm and concerning dislocated supracondylar fractures also 9 mm after 40 months This evidently contradicts the hypothesis on trial However, a comparison such as the actual one is fraught with fallacies As previously stated (p 35) there *was found a significant age difference in this material* between supracondylar fractures on the one hand, fractures through *diaphysis and surgical neck on the other* This may in itself be of minor importance since substantial differences concerning the size of overgrowth at different age periods could not be demonstrated Another question is whether the physiological (not clinical) healing time is on the same scale in *supracondylar fractures and fractures through the surgical neck If this is* not so and here data are lacking one may expect — *ceteris paribus* — that the fracture type with the slower healing will show a stronger overgrowth than is indicated by its ordinary growth potential

Other reservations could be raised such as differences in vascular anatomy between various long bones and the difficulty of comparing displacement in fractures Taken together these objections imply that the present clinical material hardly allows for a comparison aiming at a verification of the experimental results They also mean that the hypothesis propounded is neither proved nor disproved but stands open to further inquiry

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SUMMARY

At the Orthopaedic Clinic in Lund in 1955 systematic follow up investigations were begun of children who had suffered any of the following forms of humerus fractures

supracondylar fracture

diaphysis fracture

collum chirurgicum fracture

The aim was to investigate with the aid of rontgenological measurement to what extent growth stimulus after fracture in growing bone, well known in femur and tibia, also has its equivalent in humerus moreover and primarily, to map in closer detail the development of such a stimulus The intention was to find when it began and when it ended, and also to study whether the extent of the increase in growth could be set in relation to such parameters as the age of the patient, the dislocation of the fracture, and its distance from the two growth plates in humerus

The studies were carried out with orthodiagraphic measurement technique, and such measurements were intended to be made in long series with regular time intervals for as long a period as increase in growth could be demonstrated or expected Preliminary investigations during the first years showed that such growth acceleration occurred in high frequency for the first two years after the fracture, and that it could result in demonstrable differences up to 15 mm in humerus length

It proved difficult to get enough patients and to carry out a sufficient number of investigations on them Finally 86 patients who could be used for statistical analysis were obtained Of these 60 had suffered supracondylar fractures, 8 diaphysary and 18 *collum chirurgicum* The representation of the two latter categories was definitely insufficient for statistical analysis of the extent planned

The studies were carried out with simultaneous measurement of right and left humerus Because the length of the bone on the rontgen picture equalled the actual length it was possible to obtain the measurements of the two humeri and their mutual difference directly without recalculation Series of such differences in length were obtained at different times after

the fracture where in most favourable cases an initial measurement was made one month after the fracture and then with usually 3 month intervals up to 10 length recordings

After the clinical investigation was ended a somewhat inhomogeneous material was at hand of varying measuring frequency and somewhat ir regular measuring intervals The analysis of this however showed that the size of the overgrowth probably also its duration is positively correlated to the degree of dislocation A maximum for the growth acceleration could also be demonstrated 12—18 months after the fracture whereas the onset of the increase in growth could not be determined with certainty Its termination could not be established definitely but overgrowth could with some probability be shown to continue for at least 20 months

An attempt was made to appraise the possible relation of growth acceleration to age The statistical basis however was scanty and guaranteed differences between children less than 4 years of age and those more than 4 years of age could not be demonstrated

In conclusion the clinical investigation had proved

that overgrowth after humerus fracture is a very common possibly obliga tory phenomenon (frequency in this material 80 %)

that the dislocation with certainty is positively correlated to the size of overgrowth probably also to its duration

that the curve for the growth acceleration shows a maximum at 12—18 months whereas particularly its starting point could not be established and its end point in any event lay beyond 20 months possibly — for con siderably dislocated fractures — at about 3 years

that no obvious difference in growth acceleration between different age groups could be established

At the beginning of the work it was expected that a close analysis of the three different types of extraepiphyseal fractures in humerus would solve the question of the importance of the fracture level for the growth stimula tion These hopes were vain partly because of the insufficient material for this purpose and partly because an original plan to insert a metal indicator in the humerus diaphysis where it should function as a fixed point for the measurements had to be abandoned on both technical and ethical grounds

For these reasons an experimental study was motivated in order to provide information about the possible relation between fracture level and

overgrowth which could not be extracted from the clinical study A plan was devised to determine the growth rate of long bone experimentally, with the aid of oxytetracycline markings and by bone drillings equivalent to fractures, in an attempt to solve the problem

For this purpose, 404 rabbits, aged 4—5 weeks were used Tibia and radius were chosen to be operated on For each kind of bone, three different experimental series were made with drillings in the proximal metaphysis, the diaphysis, and the distal metaphysis The growth/24-hours was determined during 3 24-hour periods for the operated long bone as well as for its contralateral equivalent The investigation period included the pre operative 24-hours and the 10 following 24 hour periods

The statistical analysis of the measurement values revealed that drilling of proximal metaphysis in tibia and also in radius produced a slight increase in growth proximally and a very considerable increase distally Inversely, distal tibia drilling resulted in a strong growth acceleration proximally and almost no reaction distally Distal radius drilling did not trigger off any significant growth changes from any of the growth plates

Because two different long bones show this type of post traumatic growth reaction, and similar phenomena having been reported by other researchers this could be thought to represent a general rule not only in long bones of the rabbit but possibly also in other mammalians If an attempt is made to trace its existence in the clinical material in this study, we expect *a priori* to find a considerably larger increase in growth after supracondylar humerus fracture than after *collum chirurgicum* fracture Such a tendency is not to be found in the present material which however, because of its limited extent does not allow either a positive or a negative statement in this respect

The drillings made in the centre of the tibia diaphysis triggered off strong growth acceleration from both proximal and distal growth plates whereas corresponding drillings of radius gave similar results with considerably lower amplitude and doubtful significance

Contrary to this, the diaphysary humerus fractures in *homo* show a comparatively insignificant increase in growth This discrepancy compared with the experimental results can possibly be explained by the fractures in question often lying considerably proximally to *foramen nutritium humeri*, whereas tibia drilling was made in the immediate vicinity of *foramen nutritium tibiae* in other words, that the medullary vascular lesion at the two different types of trauma lay on different levels

In short the experimental investigation gave the following results

A drilling through cortex and medullary cavity placed at the proximal metaphysis gives a strong growth acceleration in both radius and tibia from the distal growth plate and a much slighter reaction from the proximal plate

Conversely a drilling at the distal metaphysis gives a strong reaction from the proximal growth plate of tibia and a slighter growth acceleration from the distal plate From radius a result with rather low significance however contradictory was registered

It is proposed that this mode of reaction be regarded as universal within mammalian long bones

The amount of overgrowth from a certain growth region is in all probability correlated to its natural growth potential

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Various aspects of skeletal growth have been among the foremost research problems at the Orthopaedic Clinic in Lund for about 15 years These studies, to date have resulted in six monographs (including the present work) and many articles The investigations carried out as team work were initiated and led by Professor G *Wiberg*, head of the Clinic, who undertook the task not merely by virtue of his office, but also and primarily as an active and experienced scientist I sincerely thank him for the guidance encouragement, criticism, and advice he has always willingly given even during extremely busy periods

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Laborator O *Norman* has carefully considered and criticised the roentgenological measurements Docent *S A Ahlgren B Persson* and *G Sunden* have contributed valuable suggestions and observations during the progress of the work

Fil kand L E Ek who carried out the statistical analyses readily accepted the often varying directives and tasks imposed on him

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Table 3

Avera e over rowth in mm of fractured humerus during consecutive time intervals after supracondylar fracture (disloc ++)

months from fra ture	number of obs	arithmetic mean ± stand deviation	95 % confidence interval
4—5	12	0 7±2 7(—)	0 7±1 8
8—9	24	2 6±2 6	2 6±1 0
1?—13	18	2 8±4 8	2 8±2 3
16—17	18	3 8±4 0*	3 8±1 9
—21	18	1 9±2 5	1 9±1 3
24—25	15	0 6±1 9(—	0 6±1 1
28—29	12	1 2±3 3(—	1 2±2 2
3?—33	6	1 5±2 8 —)	1.5±2 8
36—37	13	0 8±2 5 —	0 8±1 5
41—42	4	—0 8	—

Table 4

Avera e overgrowth in mm of fractured humerus during consecutive time intervals with reference to the ent re fracture material and both degrees of dislocation

months from fracture	numb r of obs	arithmet c mean ± stand d v at on	95 % confidence interval
4—5	3?	0 9±2 7(—)	0 9±1 0
8—9	52	2 1±2 6	2 1±0 8
13—14	58	2 2±3 9	2 2±1 0
16—17	30	2 4±3 8	2 4±1 4
2—1	4	0 7±1 5	0 7±0 4
4—5	47	1±2 5(—	0 1±0 8
9	26	0 6±3 0 —	0 (±1 ?
33	15	0 6±2 6(—	0 6±1 6
36—37	47	0 7±3 4 —	0 7±1 0
41—4?	9	0 3±2 8 —	0 3±2 0

Table 1

Average overgrowth in mm of fractured humerus during consecutive time intervals after fractures of the surgical neck (disloc + and ++)

months from fracture	number of obs	arithmetic mean ± stand deviation	95 % confidence interval
4— 5	7	2 8±2 3*	2 8±2 1
8— 9	8	2 0±1 2(−)	2 0±3 3
13—14	15	2 7±3 4*	2 7±1 9
22—23	8	1 4±2 3(−)	1 4±2 8
29—30	7	0 4±3 6(−)	0 4±3 4
36—37	4	1 4±1 1(−)	1 4±1 8
41—42	3	0 6±2 1(−)	0 6±5 1

Table 2

Average overgrowth in mm of fractured humerus during consecutive time intervals after supracondylar fracture (disloc +)

months from fracture	number of obs	arithmetic mean ± stand deviation	95 % confidence interval
4— 5	9	0 4±2 8(−)	0 4±2 1
9—10	14	1 4±1 7*	1 4±1 1
13—14	20	1 4±2 3*	1 4±1 1
17—18	12	0 4±2 7(−)	0 4±1 7
21—22	8	—0 6±2 3(−)	—0 6±1 9
25—26	16	—0 8±1 6(−)	—0 8±0 9
29—30	6	—0 3±1 8(−	—0 3±1 8
33—34	9	0 ±1 7(−)	0 ±1 4
37—38	6	—0 8±1 6(−)	—0 8±1 8

Table 3

Avera e over rowth in mm of fractured humerus during consecutive time intervals after supracondylar fracture (disloc ++)

months from fracture	number of obs	arithmetic mean ± stand deviation	95 % confidence interval
4—5	12	07±27(—)	07±18
8—9	24	26±26 *	26±10
1?—13	18	28±48	28±23
16—17	18	38±40	38±19
2 —21	1S	19±25	19±13
?4—25	15	06±19—)	06±11
28—?9	12	1?±33—	12±?2
3?—33	6	15±28—	15+28
36—37	1?	08±25	08±15
41—4	4	—08	—

Table 4

A erage ove growth in mm of fractured humerus during consecutive time intervals with reference to the ent re fracture mater al and both degrees of dislocation

months f om f a ture	number of obs	arithmet c mean ± stand deviation	95 % confidence interval
4—5	3?	09±27—)	09±10
8—9	52	?1±26	21±08
13—14	58	22±39	22±10
1?—17	30	24±38	24±14
— 1	4?	07±15	07±04
24—2?	47	01±25—	01±08
29	26	06±30—	06±1.2
33	15	06±26—	06±16
36—37	47	07±34—	07±10
41—4?	9	03±28—	03±20

Table 5

Yearly development of growth in control humerus

age in years	number of patients	average length of humerus in mm	standard deviation	mean standard deviation	95 % confidence interval of true mean
4	5	173.0	14.1	6.4	173.0±17.8
5	9	185.8	9.5	3.2	185.8±7.4
6	17	203.8	12.4	3.0	203.8±6.4
7	26	218.4	15.2	3.0	218.4±6.2
8	27	235.2	16.6	3.2	235.2±6.6
9	30	242.6	15.2	2.8	242.6±5.7
10	26	251.8	13.8	2.7	251.8±5.6
11	24	263.7	14.7	3.0	263.7±6.2
12	24	277.1	14.8	3.0	277.1±6.2
13	19	287.5	13.8	3.2	287.5±6.7
14	22	297.0	13.9	3.0	297.0±6.2
15	17	307.5	13.6	3.3	307.5±7.0
16	11	314.7	14.9	4.5	314.7±10.0

Table 6

TIBIA (proximal drilling)

Days (24 h)	Number of obs	arithmetic mean ± stand deviation	mean error	95 % confidence interval
Amerage daily increase in growth in μ from the proximal growth plate				
preop	23	1 ± 53 (−)	± 11	1 ± 23
1	27	24 ± 48	± 9	24 ± 18
2	28	22 ± 48*	± 9	22 ± 19
3	5	17 ± 11	± 5	17 ± 15
4	16	4 ± 32 (−)	± 8	4 ± 17
5	19	22 ± 44	± 10	22 ± 20
6	10	16 ± 25 (−)	± 8	16 ± 18
7	9	34 ± 30	± 10	34 ± 23
8	6	5 ± 16	± 7	25 ± 17
9	6	5 ± 16 −	± 7	5 ± 17
10	6	5 ± 20 (−	± 8	5 ± 20
Average daily increase in growth in μ from the distal growth plate				
preop	19	8 ± 78 −	± 18	8 ± 38
1	26	19 ± 41	± 8	19 ± 17
2	22	25 ± 52	± 10	25 ± 20
3	10	45 ± 28	± 9	45 ± 21
4	15	42 ± 35	± 9	42 ± 19
5	21	44 ± 27	± 6	44 ± 13
6	12	10 ± 24	± 7	10 ± 15
7	9	21 ± 24	± 8	21 ± 19
8	6	13 ± 10	± 4	13 ± 10
9	6	3 ± 1 (−	± 5	3 ± 13
10	6	− 8 ± 12 −)	± 5	− 8 ± 13

Table 7

TIBIA (mid diaphyseal drilling)

Days (24 h)	Number of obs	arithmetic mean ± stand deviation	mean error	95 % confidence interval
Amerage daily increase in growth in μ from the proximal growth plate				
preop	14	− 7 ± 56(−)	± 15	− 7 ± 32
1	21	24 ± 50*	± 11	24 ± 23
2	22	31 ± 42**	± 9	31 ± 19
3	3	60 ± 31(−)	± 18	60 ± 77
4	8	51 ± 42**	± 15	51 ± 35
5	10	63 ± 38***	± 12	63 ± 27
6	9	58 ± 65*	± 21	58 ± 48
7	4	45 ± 24*	± 12	45 ± 38
8	6	38 ± 32	± 13	38 ± 33
9	6	18 ± 36*	± 15	18 ± 39
10	6	15 ± 41(−)	± 17	15 ± 44
Average daily increase in growth in μ from the distal growth plate				
preop	17	22 ± 25**	± 6	22 ± 12
1	23	30 ± 24***	± 5	30 ± 10
2	23	29 ± 24 **	± 5	29 ± 11
3	3	66 ± 9**	± 5	66 ± 20
4	10	61 ± 22* *	± 7	61 ± 16
5	11	67 ± 20 **	± 6	67 ± 14
6	10	39 ± 28*	± 9	39 ± 21
7	3	25 ± 7*	± 4	25 ± 18
8	6	23 ± 33(−	± 13	23 ± 33
9	6	22 ± 34 −	± 14	22 ± 36
10	6	18 ± 32 −)	± 13	18 ± 33

Table 8

TIBIA (distal drilling)

Days 24 (h)	Number of obs	arithmetic mean ± stand deviation	mean error	95 % confidence interval
Average daily increase in growth in μ from the proximal growth plate				
preop	23	0±43(–)	± 9	0±19
1	37	22±51	± 9	22±18
2	30	27±44 *	± 8	27±16
3	6	74±42	±17	74±44
4	12	53±45	±13	53±29
5	14	55±34	± 9	55±19
6	10	24±16	± 5	24±11
7	9	8±39 –	±13	8±30
8	11	12±37 –	±10	12±22
9	10	21±31 –	±10	21±23
10	5	30±29 –	±13	3[illegible]±36
Average daily increase in growth in μ from the distal growth plate				
preop	20	14±18	± 4	14± 9
1	8	12±21	± 4	1[illegible]± 8
2	30	± –	± 4	2± 8
3	5	– 8±22 –	±10	– 8±27
4	11	0±26 –	± 8	0±19
5	15	15±23	± 6	15±1[illegible]
6	11	0±17 –	± 5	0±12
7	8	22±11	± 4	22± 9
8	11	19±35 –	±11	19±25
9	10	14±2[illegible] (–)	± 6	14±1[illegible]
10	5	12±13(–)	± 6	1[illegible] ±17

Table 9

RADIUS (proximal drilling)

Days (24 h)	Number of obs	arithmetic mean ± stand deviation	mean error	95 % confidence interval
Average daily increase in growth in μ from the proximal growth plate				
preop	13	8 ± 14(—)	± 4	8 ± 9
1	15	21 ± 19**	± 5	21 ± 11
2	16	13 ± 28(—)	± 7	13 ± 15
3	5	2 ± 22(—)	± 10	2 ± 28
4	2	—15	—	—
5	8	—14 ± 27(—)	± 8	—14 ± 19
6	8	1 ± 34(—)	± 12	1 ± 28
7	8	9 ± 31(—)	± 11	9 ± 26
8	3	— 3 ± 19(—)	± 11	— 3 ± 47
9	4	— 2 ± 16(—)	± 8	— 2 ± 25
10	6	21 ± 32(—)	± 13	21 ± 33
11	5	25 ± 40(—)	± 18	25 ± 50
Average daily increase in growth in μ from the distal growth plate				
preop	10	11 ± 22(—)	± 7	11 ± 16
1	14	21 ± 30*	± 8	21 ± 17
2	17	39 ± 37***	± 9	39 ± 19
3	5	38 ± 20*	± 9	38 ± 25
4	4	49—	—	49 ± 4
5	5	43 ± 33*	± 15	43 ± 42
6	12	33 ± 24***	± 7	33 ± 15
7	12	27 ± 35*	± 10	27 ± 22
8	5	13 ± 51(—)	± 23	13 ± 64
9	5	15 ± 47(—)	± 21	15 ± 58
10	2	12	—	—

Table 10

RADIUS (mid diaphyseal drilling)

Average daily increase in growth in μ from the proximal growth plate				
Days (24 h)	Number of obs	arithmetic mean ± stand deviation	mean error	95 % confidence interval
preop	2	0	—	—
1	5	16 ± 27 (−)	± 12	16 ± 33
2	6	14 ± 58 (−	± 24	14 ± 62
3	7	11 ± 32 (−)	± 12	11 ± [illegible]9
4	4	5 ± 18 (−)	± 9	5 ± 28
5	6	− 2 ± 27 −)	± 11	− 2 ± 28
6	8	20 ± 48 −	± 17	20 ± 40
7	9	18 ± [illegible]6 −	± 22	18 ± 50
8	6	17 ± 46 −	+ 19	17 ± 52
9	6	10 ± 58 (−	± 24	10 ± 66
10	6	2 ± 66 −	± 27	22 ± 74
Average daily increase in growth in μ from the distal growth plate				
preop	2	4	—	—
1	4	20 ± 8	± 4	20 ± 14
2	3	36 ± 16 (	± 9	36 ± 37
3	5	22 ± [illegible] −	± 9	22 ± 24
4	4	38 ± 26 −)	± 13	38 ± 41
5	4	2 ± 12 −	± 6	2 ± [illegible]
6	6	− 7 ± [illegible]9 (−	± 12	− 7 ± 30
7	10	3 ± 38 −	± 12	3 ± 28
8	5	7 ± 22 −	± 10	[illegible] ± 27
9	3	3 ± 7 −	± 4	3 ± 18

9

Table 11

RADIUS (*distal drilling*)

Days (24 h)	Number of obs	arithmetic mean ± stand deviation	mean error	95 % confidence interval
Average daily increase in growth in μ from the proximal growth plate				
preop	19	$5 \pm 26^{(-)}$	±6	5±13
1	24	$0 \pm 29^{(-)}$	±6	0±12
2	25	$10 \pm 20^{*}$	±4	10± 8
3	10	$4 \pm 12^{(-)}$	±4	4± 9
4	7	$-4 \pm 19^{(-)}$	±7	−4±17
5	13	$-2 \pm 14^{(-)}$	±4	−2± 9
6	16	$0 \pm 20^{(-)}$	±5	0±11
7	18	$6 \pm 17^{(-)}$	±4	6± 8
8	10	$8 \pm 19^{(-)}$	±6	8±14
9	13	$13 \pm 14^{**}$	±4	13± 9
10	9	$16 \pm 27^{(-)}$	±9	16±21
11	7	$10 \pm 21^{(-)}$	±8	10±20
Average daily increase in growth in μ from the distal growth plate				
preop	17	$10 \pm 25^{(-)}$	± 6	10±13
1	21	$15 \pm 27^{*}$	± 6	15±13
2	23	$30 \pm 36^{*\ *}$	± 7	30±15
3	9	$36 \pm 72^{(-)}$	±24	36±45
4	7	$9 \pm 52^{(-)}$	±20	9±49
5	13	$2 \pm 32^{(-)}$	± 9	2±20
6	15	$3 \pm 27^{(-)}$	± 7	3±15
7	12	$9 \pm 41^{(-)}$	±12	9±26
8	9	$9 \pm 42^{(-}$	±14	9±32
9	8	$8 \pm 56^{-}$	±20	8±47
10	3	17	—	—

Table 1

Change in growth in *control* bone expressed in microns and referring to the 1st and 2nd postoperative 24 hour periods in relation to the preoperative period

TIBIA (proximal drilling)

a) proximal growth plate

24 hour periods	number of obs	mean ± stand deviation	mean error	95 % confidence interval
1 postop	27	−27 ± 31	± 6	−27 ± 12
2 postop	27	−34 ± 46 *	± 9	−34 ± 18

b) distal growth plate

1 postop	24	−38 ± 34	± 7	−38 ± 14
2 postop	23	−24 ± 44	± 9	−24 ± 19

TIBIA (mid diaphyseal drilling)

a) proximal growth plate

1 postop	17	−19 ± 33	± 8	−19 ± 17
2 postop	17	−15 ± 39(−)	± 9	−15 ± 20

b) distal growth plate

1 postop	19	−22 ± 63 −	± 14	−22 ± 30
2 postop	19	− 5 ± 52 −)	± 12	− 5 ± 25

TIBIA (distal drilling)

a) proximal growth plate

1 postop	28	−30 ± 38	± 7	−30 ± 15
2 postop	28	−47 ± 52	± 10	−42 ± 20

b) distal growth plate

1 postop	25	−32 ± 35	± 7	−32 ± 15
postop	25	−26 ± 45	± 9	−26 ± 19

Table 11

RADIUS (distal drilling)

Days (24 h)	Number of obs	arithmetic mean ± stand deviation	mean error	95 % confidence interval
Average daily increase in growth in μ from the proximal growth plate				
preop	19	$5 \pm 26^{(-)}$	±6	5±13
1	24	$0 \pm 29^{(-)}$	±6	0±12
2	25	$10 \pm 20^{*}$	±4	10± 8
3	10	$4 \pm 12^{(-)}$	±4	4± 9
4	7	$-4 \pm 19^{(-)}$	±7	− 4±17
5	13	$-2 \pm 14^{(-)}$	±4	− 2± 9
6	16	$0 \pm 20^{(-)}$	±5	0±11
7	18	$6 \pm 17^{(-)}$	±4	6± 8
8	10	$8 \pm 19^{(-)}$	±6	8±14
9	13	$13 \pm 14^{**}$	±4	13± 9
10	9	$16 \pm 27^{(-)}$	±9	16±21
11	7	$10 \pm 21^{(-)}$	±8	10±20
Average daily increase in growth in μ from the distal growth plate				
preop	17	$10 \pm 25^{(-)}$	± 6	10±13
1	21	$15 \pm 27^{*}$	± 6	15±13
2	23	$30 \pm 36^{***}$	± 7	30±15
3	9	$36 \pm 72^{(-)}$	±24	36±55
4	7	$9 \pm 52^{-}$	±20	9±49
5	13	$2 \pm 32^{(-)}$	± 9	2±20
6	15	$3 \pm 27^{(-)}$	± 7	3±15
7	12	$9 \pm 41^{(-)}$	±12	9±26
8	9	$9 \pm 42^{(-}$	±14	9±32
9	8	$8 \pm 56^{(-)}$	±20	8±47
10	3	17	—	—

Table 13

SHAM OPERATIONS

TIBIA (Proximal growth plate)

Source of variation	Degrees of freedom	SS	MS	F quotient
Between animals	4	15 73	3 93	8 19
Between days	2	0 13	0 07	0 01 (–)
Residual	8	3 87	0 48	
Total	14	19 73		

TIBIA (Distal growth plate)

Source of variation	Degrees of freedom	SS	MS	F quotient
Between animals	4	67 73	16 93	17 28*
Between days	2	4 13	2 07	2 11 (–)
Residual	8	7 87	0 98	
Total	14	79 73		

RADIUS (proximal drilling)

a) proximal growth plate

1 postop	12	$-9\pm18^{(-)}$	±5	-9 ± 12
2 postop	12	$-6\pm14^{(-)}$	±4	-6 ± 9

b) distal growth plate

1 postop	14	$-27\pm44^{*}$	±12	-27 ± 25
2 postop	13	$+20\pm52^{(-)}$	±14	$+20\pm31$

RADIUS (distal drilling)

a) proximal growth plate

1 postop	20	$-8\pm14^{*}$	±3	-8 ± 7
2 postop	20	$-1\pm12^{(-)}$	±3	-1 ± 6

b) distal growth plate

1 postop	21	$-30\pm38^{**}$	±8	-30 ± 17
2 postop	21	$-11\pm45^{(-)}$	±10	-11 ± 20



VEIJO A RITSILÄ

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I INTRODUCTION
PURPOSE OF THE INVESTIGATION

Despite the increase in our knowledge of various malformations the etiology of many common deformities such as club foot and vertical talus remains unknown Detailed patho-anatomical observations have not led to the solution of the problems of the etiology and pathogenesis of talipes equinovarus The reason for such divergence may be that there have been differences of etiology in different cases But in such clinical and patho-anatomical studies it is difficult especially at late stages to distinguish secondary changes from primary It is also evident that in congenital deformities different etiological factors may lead to similar structural changes The orthopedic treatment of deformities however aims at the correction of changes in the musculo skeletal system or the prevention of their progression or recurrence Thus information on the nature of the peripheral deforming mechanism may be of great importance in planning effective treatment

In a study concerning the development and pathogenesis of the experimental dislocation of the hip in the rabbit *Langenskiold et al* (1962) emphasized some of the basic principles of teratology in the following statement We know that by altering the environment of the embryo we can produce abnormalities simulating those of genetic origin We know too that the nature of the alteration or injury is less important in determining the result than its site of action and the stage in embryonic development at which it is applied Since the development of the skeletal tissue continues after birth it is possible to extend this statement to postnatal developmental events as well Thus conditions simulating true congenital defects may result from injurious environmental factors affecting the child after the intrauterine period

Congenital skeletal deformities in humans may have a genetic origin as a rule But in children we see infections and injuries damaging growing bones and producing deformities similar to those of genetic origin Observations of foot deformities caused by poliomyelitis and certain

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patho anatomical studies of congenital foot deformities have given many investigators reason to suppose that soft tissue anomalies in some way cause bone deformity On this basis it seems reasonable to try to imitate experimentally conditions which have been shown to result from abnormalities of the germ plasm

Therefore the purpose of the present study was

— to investigate whether it is possible to produce foot deformities in newborn rabbits phenotypically similar to human congenital deformities especially talipes equinovarus deformity by means of various surgical and non surgical soft tissue procedures

— to carry out a detailed anatomic study of deformities produced by these procedures

— to elucidate the peripheral deforming mechanism in congenital foot deformities by comparing observations in humans with experimental results achieved

II REVIEW OF LITERATURE

A TALIPES EQUINOVARUS

1 Etiology

The first etiological theory was that of *Hippocrates* (*Kite* 1964) He believed that club-foot was the result of intra uterine pressure This idea has been elaborated with convincing arguments by *Denis Browne* (1933 1936 1967) Many others have returned to the notion that intra uterine position or mechanical factors may be the cause of club foot (*Parker* and *Schattock* 1884 *Keith* 1897 *Nutt* 1925)

Club-foot has also been considered to be secondary to a lesion of the external popliteal nerve caused by pressure at the intra uterine stage (*White* 1929) Another neurological theory of the cause of club foot is that it might result from a nerve lesion similar to deformities which result in nerve lesions after birth (*Little* 1839 *Adams* 1873) *Chapman* (1839) wrote Club-foot originates in the nerves supplying the flexor and extensor muscles of the foot *Nutt* (1925) also mentioned as one etiological possibility of the cause of the club-foot a nerve anomaly A primary defect of the spinal cord has also been considered to be the cause of club-foot (*Courtiller* 1897 *Dittrich* 1930)

The part played by heredity was stressed by *Aschner* and *Engelmann* in 1928 and by many since *Compere* (1951) considered hereditary factors leading to neuromuscular imbalance as a cause of club-foot

Disturbances in the development of striated muscle fibres (*Middleton* 1932) a primary muscular defect (*Smith* 1948) an imbalance of muscles resulting from their hypo- or hypertonicity (*Lombard* 1950 and 1952) a primary muscular imbalance due to dysplasia of the peroneals (*Flinchum* 1953) a relative shortening of degenerating muscle fibres during growth (*Bechtol* and *Mossman* 1950) are muscular changes on which the blame has been laid for the origin of club-foot

That the activity of the anomalously inserted muscles can lead to foot deformity has been suggested by many authors (*Scherb* 1930 *Stewart* 1951 *Fredenhagen* 1955 *Irelan* 1958 and 1960)

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That the activity of the anomalously inserted muscles can lead to foot deformity has been suggested by many authors (*Scherb* 1930 *Stewart* 1951 *Fredenhagen* 1955 *Inclan* 1958 and 1960)

Wiley (1959) thought the primary cause of club foot was an extrinsic factor maintaining the foot in a deformed position and causing deficiencies in the growth of the leg muscles

According to one theory the cause of club foot was developmental inhibition or arrested development at the embryological stage when muscles tendons and joints develop (*Bessel-Hagen* 1889 *Ketch* 1892 *Bohm* 1929 *Schinz et al* 1952 *Tripp* and *Shaw* 1967)

The hypothesis that club foot is due to congenital dislocation of the head of the talus has been advanced by *Brockman* (1930 1937) Also *Reimann* (1967) believed that congenital club foot is a deformity of local nature caused by primary dislocation between the tarsal navicular and the head of the talus during fetal life

Mesenchymal dysplasia in the medial part of the foot has been considered the mechanism of club foot (*Keith* 1940) Changes in connective tissues have also been suggested as the cause of club foot by others (*Scheel* 1951 *Ode* 1952)

2 Pathological anatomy

Patho anatomical observations of foot deformities have been made at autopsy since antiquity and operative examination has become common during the last few decades But dissection of fetal and immediately postnatal club foot in order to determine primary changes of the intra uterine period has not been seriously undertaken until very recent times After the first few years of life secondary adaptive changes lead to a confusing picture

Formerly the pathology of congenital skeletal deformities was studied almost entirely from the bone deformity point of view and the skeletal changes were considered primary Nowadays however the belief is widespread that pathological changes in the muscle-tendon apparatus precede and even initiate bone changes

a) *Bone changes*

After examining the bones of children with club foot some 165 years ago *Scarpa* believed that the deformity was due to medial twisting of the navicular cuboid and calcaneus in relation to the talus The talus itself was considered normal in shape and position Muscle abnormalities were considered secondary *Adams* (1873) asserted that the essential change involved in idiopathic club foot occured in the tarsus He found the principal deformity in the talus particularly in the neck and head of the

talus *Scudder* (1887) noted that the neck of the astragalus turned inward instead of being straight In the 19th century there were several German accounts of club-foot dissection with particular elucidation of bone changes (*Hueter* 1863 *Kocher* 1878 etc) Similar work was done by *Parker* and *Schattock* (1884) who noted talar deformity as did the Russian *Sherbunenko* (1899)

Burrell (1893) found no important muscle changes in a seven month fetus with a club foot He found bone changes however and said The astragalus of the deformed foot was small and its neck short The outer part of the articular surface of the deformed astragalus as it articulated with the scaphoid was distinctly diminished in size

Nichols (1897) in his dissection of a stillborn child with club feet noted only directional changes and shortening in the tendons of tibialis anterior posterior and gastrocnemius He stated The deformity of the foot in cases of congenital equinus is due essentially to an alteration in the shape of the bones of the foot The greatest and most important abnormalities are the obliquity of the facets and the change in the shape of the bones which enter into the information of the midtarsal joint that is the astragalus and the os calcis posteriorly and the scaphoid and cuboid anteriorly All the bones are altered

Until quite recently in fact the main emphasis in dissection reports was placed on bony changes in congenital foot deformity This was the case in dissections performed by *Elmslie* (19 0) and *Pfranr* (19-0) *Bohm* (1935) also noted that the soft tissues were normal and the equino varus foot depended upon serious deformities of the talus and calcaneus In their publications and monographs *Kreu* (1927) *Mau* (1927) *Virchow* (1933) *Debrunner* (1936) *Bernbeck* (1950 1955) and *Schlicht* (1963) have described in detail the bone changes of talipes equinovarus with emphasis on changes of shape in the talus and its joint surfaces to which other tarsal bones (cuboid navicular and calcaneus) adapt themselves with lesser changes

Three careful studies of the anatomy of club-foot in fetuses and still born children have been published very recently *Irani* and *Sherman* (1963) examined eleven cases of club-foot and three calcaneo-valgus foot Their conclusions were In idiopathic club foot there are no primary abnormalities of vessels nerves muscles or tendon insertions Only the anterior part of the talus *is always* abnormal The anterior part of the calcaneus is usually abnormal but much less so and to variable degree These deviations probably result from a defective cartilaginous anlage which is dependent upon a primary germ plasm defect *Settle* (1963)

presented his anatomical findings from the dissection of sixteen infantile club-feet Anatomical abnormalities were surprisingly uniform He writes congenital talipes equinovarus is a composite deformity involving all tissues of the foot There are no simple or isolated defects such as *contracted bands or peroneal muscle atrophy* but each tissue conforms to the equinus and varus position The major bone deformity resides in the talus Its neck and articular surface for the navicular deviate to face medially and plantarward Congenital club foot is a primary developmental deformity of the hind part of the foot *Reimann* (1967) presented the dissection material of six cases comprising fetuses still borns and persons with club foot who had died Her conclusions were Gross and histological studies of the spinal cord and nerve roots including ganglion cell counts disclosed no abnormality in the club foot cases Histological study of muscles showed no signs of neurogenous atrophy Histological study of the muscles showed normal muscles Microscopically the average diameter of the muscle fibres was diminished Histologically the vessels have proved normal Skeletal changes have been a constant finding *consisting of dysplasia and changes in shape* mostly affecting the talus The skeletal changes are considered to be secondary

b) Soft tissue changes

Little (1839) was the first to assert that uncoordinated muscle activity or abnormal tendon insertions might be the cause of club foot and mentions the notion of Hippocrates that muscles maintain the clubfoot *Mackeever* (1820) (quoted by *Little*) and *Tourtual* (1832) had made earlier *observations on muscles in this connection*

Adams (1854—1855) described the dissection of immediately post natal cases of club foot and discovered anomalies in the gastrocnemius the tibialis anterior and the tibialis posterior muscles which were very tense and possibly hypertrophied *All three muscle bellies were shor*tened The extensor digitorum longus muscle was very small and microscopically degenerate In another case he found several tendinous abnormalities Nevertheless he considered soft tissue changes to be secondary and was convinced that the talus changes he had found were primary

Von Volkmann (1865) also described changes in the muscles of club foot and noted small peroneal *muscles* and a *small* extensor digitorum communis muscle

Bissell (1888) studied the muscles of the equinovarus feet of an infant and noted that the tibialis anterior and posterior tendons had

shortened and moved inwards Like many other investigators however he was more deeply concerned with detailed description of bone changes especially in the talus

Elmslie (1920) discussed the anatomy of the club-foot He wrote that the chief factor of the deformity was a displacement of the bones and that the importance of the tendons in maintaining a deformity had been much exaggerated But he also said Doubtless the tendons of the tibialis anticus and posticus and tendo Achillis have a considerable part in the original production of the deformity

Dittrich (1930) published the results of a dissection of an infant with bilateral club-foot and came to the conclusion that the position and form of the various components of the foot are secondary to changes in the soft tissues which control them

Middleton (1932) studied the pathological anatomy of congenital anomalies and assembled material which included congenital tibial kyphosis and arthrogryposis multiplex congenita He suggested the imperfect development of striated muscle as a possible cause of certain congenital deformities of the extremities

Mau (1938) made an examination of three fetuses with club-foot and other congenital abnormalities In muscles he found macroscopically nothing of note but histologically there was a loss of striation He considered this secondary to myelodysplasia He noted changes in each muscle of his histological specimen and could not attribute the deformity to any particular muscle

Scherb (1930) also noted anomalies in club foot muscles In operations he often noticed an attachment of the peroneus brevis muscle to the cuboid instead of the usual attachment to the fifth metatarsal This he asserted was the cause of a depression of the lateral edge of the foot and a relative increase of supination power due to the abductive effect of the peroneus brevis muscle on the metatarsal plate decreased Similar changes in the lateral tendinous region have been noted by *Debrunner* (1957) and also by *Fredenhagen* (1954)

Bechtol and *Mossman* (1950) studied embryonic club foot and observed changes in muscular development some cases being more imperfectly developed in the histological sense This the authors maintained was the cause of the muscular imbalance of club-foot

Stewart (1951) presented his findings from the dissection of one stillborn and twenty operated patients He found several abnormalities of tendon insertion but most common was the unusual attachment of the Achilles tendon to the medial side of the tuber calcanei His findings were in full

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agreement with the results presented earlier by Scherb In 1954 *Penners* published similar insertion anomalies noted in operated patients They occurred in Achilles tendon insertions in the tibialis anterior and extensor hallucis longus tendons in the plantaris muscle in the insertion of the tibialis posterior tendon and in the plantar fascia

Flinchum in 1953 published the results of his dissection of a club-foot in a six and a half month infant He found an insertion anomaly of the Achilles tendon a large tibialis anterior muscle and small peroneal muscles The tibialis posterior muscle was normal compared to the standard of a healthy foot The author considered bone changes secondary resulting from muscular imbalance

Wiley (1959) gathered material in six cases of club-foot from post mortem examinations performed on infants He noted that the bellies of the long muscles were shorter and thinner and commented In the severe cases abnormal musculature was noted throughout the long muscles In talipes equinovarus the principal muscles affected were the gastrocnemius and soleus the tibialis posterior and the tibialis anterior in that order The cause of these muscle changes in his opinion was an extrinsic factor maintaining the foot in a deformed position and causing growth deficiencies in the long muscle

B VERTICAL TALUS

The congenital flat foot deformity connected with the vertical position of the talus received no attention in the literature until this century The vertical position had evidently remained unnoticed and vertical talus cases had been discussed in connection with ordinary flat foot cases It was the development of the X ray technique which made a consideration of the various forms of flat foot possible

The first complete radiological anatomical and pathological study of extreme flat foot with vertical talus dates from 1914 (*Henken*) Numerous publications followed in which the deformity was described They were mainly from continental Europe in the period 1920—40 All authors noted the special features of the deformity These are clinically convexity of the sole deviation into valgus of the posterior part of the foot abduction and dorsiflexion of the forepart of the foot and radiographically, the vertical or oblique position of the talus

There have been divergent opinions on the nature of the deformity however some considering it a specific congenital malformation (*Chrysospathes* 1938) and others not considering it a morbid entity (*Ombrédanne*

1928) It has been recognized by most authors recently as an individual entity (*Herndon* and *Heyman* 1963) The latter used the term congenital convex pes valgus which was first used in 1939 by *Lamy* and *Weissman* who list nine other terms in use The terms vertical talus or congenital talonavicular dislocation or subluxation are recent additions All these reflect different points of view in the interpretation of this deformity

As with the etiology and pathology of talipes equinovarus deformity there are a great variety of corresponding theories on the etiology and pathogenesis of congenital flat foot and congenital vertical talus deformity They can be divided into exogenic or extrinsic and endogenic or intrinsic theories

Many have believed congenital flat foot is an exogenic malformation caused by intra uterine pressure (*Henke* 1859 *Kustner* 1880 *Joachimsthal* 1903 *Lange* 1912 *Henken* 1914 *Krukenberg* 1934—1935 *Denis Browne* 1966 *Harrold* 1967) According to *Murk Jansen* (quoted by Spiro 1934—1935) pressure arises from a deficiency of amnion *Chrysospathes* (1938) thought that pressure of the tibia against the tarsal bones in the early embryonic stage with the foot in dorsiflexion would cause deformity

Many factors have been suggested which support the theory of endogenic origin The deformity is often accompanied by other congenital malformations such as congenital luxation of the hip club foot arthrogryposis spina bifida congenital kyphosis hypospadia and microcephaly Some have found evidence of heredity in this condition (*Aschner* and *Engelmann* 1928) Also congenital talus verticalis has certain features in common with certain stages of the normal embryogenic development of the foot Various authors consider that disturbed development of the bones of the foot is the primary reason for the deformity as in club foot

Franke (1901) considered disturbances of muscle balance to be the cause of congenital flat foot He asserted that the insertion of the tibialis anterior had moved from the plantar to the dorsal side and that its supinatory effect was thus eliminated *Braus* (quoted by *Lamy* and *Weissman* 1939) has noted in 50 per cent of congenital flat foot cases that the supinatory effect of the tibialis anterior is lacking because of insertion variation According to *Lamy* and *Weissman* *Mau* pursuing the same line of thought assumed that a spinal lesion could cause a predominance of peroneal muscle action at a certain stage of fetal development leading to a valgus position of the foot

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Lamy and *Weissman* (1939) state that all explanations of congenital pes valgus are far from satisfactory and the cause is still to be found It should be sought among endogenous factors however since external factors only occasionally intervene The role of the nervous system appears to be the most important This is their opinion of the pathogenesis of club foot in general

Hark (1950) emphasized two facts concerning the etiology one is the multiplicity of other deformities accompaning rocker foot and the other is the occurence of only one case of spina bifida in his series He believes that spina bifida is merely one manifestation of a developmental disturbance which may include rocker foot as well as other deformities

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C EXPERIMENTAL PRODUCTION OF SKELETAL MALFORMATIONS

The etiology of congenital defects in human beings is virtually unknown and evidently both genetic and environmental influences are involved (*Kalter* 1965 *Saxen* and *Rapola* 1969) For many years congenital anomalies were generally assumed to be wholly due to defects of the genes chromosomes and germ plasm Genetic considerations have tended to overshadow the importance of the environmental influences (*Ingalls* 1955) However the association of developmental anomalies with epidemics of rubella noted first in Australia by *Gregg* (1941) and attributed to maternal infection in the early months of pregnancy by *Swan* (1949) demonstrates clearly enough that changes in the genome cannot always be invoked as the cause of congenital abnormalities Systematic studies of the congenital anomalies demonstrates that part of them are hereditary genotypic but also that environmental factors have teratogenic influence The recent appearance of newborn babies with malformed limbs due to maternal ingestion of thalidomide as a tranquilizing drug during pregnancy has revealed the sensitivity of the fetus to these teratogenic factors (*Len* and *Knapp* 1962)

Experimental teratology has made great progress in the last few years and many excellent articles have been written on the experimental production of malformations (*Fraser* 1964 *Sal geber* and *Wolff* 1964 *Saxen* and *Rapola* 1969) The list of exogenous factors causing skeletal malformations in experimental animals is long and includes mechanical injuries hypoxia ionizing radiation a great variety of chemical compounds dietary deficiences hormonal factors virus inoculation etc Such factors may act on a genetically normal embryo causing different skeletal anomalies but several examples have been described in which synergistic effect with a mutant gene has been demonstrated (Fraser *Walker* and *Trasler* 1957 *Landauer* 1965 *Dagg* 1967) Only a few pioneering experiments in this field have been chosen for discussion and reader is referred to recent articles where the problem has been dealt with in greater detail

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(1952) and later *Degenhardt* and *Knoche* (1959) have published detailed material on the skeletal defects in the offspring of mothers subjected to low oxygen pressures

Ionizing radiation has been used for the experimental provocation of congenital deformities The first experiments on mammals were carried out in pregnant rabbits by v *Hippel* in 1905 In 1920—29 *Bagg* published his important studies He investigated the effect of X rays radium emanation and injections of radio active solutions on the development of mice rats and dogs The most constant lesions occurred in the head region of embryos There were also abnormalities of the limbs various forms of club foot syndactylism hypodactylism congenital amputations and polydactylism Later *Warkany* and *Schraffenberger* (1947) in rats and *Russel* and *Russel* (1954) in mice produced primarily skeletal anomalies by X-ray irradiation

Chemoteratogenesis the production of malformations by means of chemical substances has after the thalidomide disaster attracted much interest Many active teratogens both naturally occurring and artificially produced have since been described However as early as 1921 *Stockard* published a classic study in which he succeeded in reproducing malformations by means of chemical agents The work of *Ancel* and *Lallemand* (1942) has contributed considerably to the development of experimental teratology They succeeded in producing malformations of chick embryos by eserine sulphate and sulphonamide Since then a great variety of chemical compounds have been tested for their teratogenic action and in most cases a suitable combination of dose and animal species have yielded positive results As regards human development proven chemical teratogens are however few (*Cahen* 1966) The thalidomide accidents prompted a large number of investigators to test thalidomide in various animal species In mice and rabbits it had a teratogenic effect The first experiments were carried out by *Giroud Tuchmann-Duplessis* and *Mercier-Parot* (1962) With regard to the limbs the most common findings were malformations of the club foot type *Drachman* and *Coulombre* (1962) induced club feet and arthrogryposis curarizing chick fetuses

Dietary deficiencis have a teratogenic effect The first research on vitamin deficiencis was carried out by *Hale* (1933) He produced eye anomalies in pigs by vitamin A deficiency *Warkany* and *Nelson* (1940) used the deficiency of riboflavin in the mother s diet to induce experimentally skeletal malformations like many other anomalies Deficiency

of folic acid panthotenic acid and vitamin E have also been used to produce skeletal anomalies cleft palate club-foot etc

Hormonal factors can also induce experimental malformations Insulin has a strong teratogenic effect on the limb in the chick embryo (*Landauer* 1945) Very interesting studies to orthopedic surgery were carried out by *Duraiswami* (1952) who induced congenital skeletal defects in chick embryos also by insulin Using certain pituitary preparations *Jost* (1953) obtained degeneration of the extremities in the rat fetus Cortisone has been used as a teratogenic agent by many *Hicks* (1954) provoked among other defects skeletal anomalies by large cortisone doses in mice The investigations of *Walker* and *Fraser* (1956 1957) who induced cleft palate deformity by cortisone both in mice and rats are classical

In experimental teratology many other environmental agents such as virus infection have been used to produce congenital anomalies By mean of influenza A virus in chick embryos *Hamburger* and *Habel* (1947) provoked a typical anomaly microcephaly and *Ferm* and *Kilham* (1964) induced congenital anomalies in hamster with H 1 virus

Intra uterine manipulations have also been used in experimental teratology Some recent experiments in which embryos have been treated locally *in utero* may prove very important *Schinckel* and *Ferguson* (1963) performed skin graftings on fetal lambs for studying the development of the immune system In 1964 *Spencer* and *Pellier* reported their attempts utilizing *in utero* surgical procedures to produce a deformity in the fetal rabbit extremity By means of a silk suture a fore foot was placed in a moderate degree of flexion and ulnar deviation On the day of delivery the suture was removed from the extremity and the rabbit observed for deformity

Postnatal experimental production of skeletal deformities by transection of muscles and ligaments by denervation of muscles and by bone or joint procedures has been described in scoliosis dislocation of hip etc (*Schwartmann* and *Miles* 1945 *Langenskiold* *Sarpio* and *Michelsson* 196_ *Michelsson* 1965) However I have not found in the literature a single such report concerning experimental production of limb deformity

(1952) and later *Degenhardt* and *Knoche* (1959) have published detailed material on the skeletal defects in the offspring of mothers subjected to low oxygen pressures

Ionizing radiation has been used for the experimental provocation of congenital deformities The first experiments on mammals were carried out in pregnant rabbits by v *Hippel* in 1905 In 1920—29 *Bagg* published his important studies He investigated the effect of X-rays radium emanation and injections of radio active solutions on the development of mice rats and dogs The most constant lesions occurred in the head region of embryos There were also abnormalities of the limbs various forms of club foot syndactylism hypodactylism congenital amputations and polydactylism Later *Warkany* and *Schraffenberger* (1947) in rats and *Russel* and *Russel* (1954) in mice produced primarily skeletal anomalies by X-ray irradiation

Chemoteratogenesis the production of malformations by means of chemical substances has after the thalidomide disaster attracted much interest Many active teratogens both naturally occurring and artificially produced have since been described However as early as 1921 *Stockard* published a classic study in which he succeeded in reproducing malformations by means of chemical agents The work of *Ancel* and *Lallemand* (1942) has contributed considerably to the development of experimental teratology They succeeded in producing malformations of chick embryos by eserine sulphate and sulphonamide Since then a great variety of chemical compounds have been tested for their teratogenic action and in most cases a suitable combination of dose and animal species have yielded positive results As regards human development proven chemical teratogens are however few (*Cahen* 1966) The thalidomide accidents prompted a large number of investigators to test thalidomide in various animal species In mice and rabbits it had a teratogenic effect The first experiments were carried out by *Giroud Tuchmann-Duplessis* and *Mercier-Parot* (1962) With regard to the limbs the most common findings were malformations of the club foot type *Drachman* and *Coulombre* (1962) induced club feet and arthrogryposis curarizing chick fetuses

Dietary deficiencis have a teratogenic effect The first research on vitamin deficiencis was carried out by *Hale* (1933) He produced eye anomalies in pigs by vitamin A deficiency *Warkany* and *Nelson* (1940) used the deficiency of riboflavin in the mother s diet to induce experimentally skeletal malformations like many other anomalies Deficiency



FIG X rays in the lateral projection of the normal foot of a man (top) and of a rabbit (bottom) General skeletal structure and relative positions of bones are strikingly similar

B ANATOMY OF THE FOOT OF THE RABBIT COMPARED WITH THE HUMAN FOOT

The human foot is unlike any other It is the most distinctly human part of the whole of man s anatomical make up It is by his feet that man is distinguished from all other members of the animal kingdom (*Jones* 1944)

Despite this however there are remarkable resemblances between the hind feet of quadrupeds and the human foot The resemblance is of course greatest in anthropoid apes but the use of such large and expensive animals in the study of foot deformities would present difficulties if a sufficiently large material were to be obtained In many other four

III MATERIAL AND METHODS

A EXPERIMENTAL ANIMALS

The present study is based on the results of operations on 402 growing rabbits Approximately 75 100 growing rabbits were used in preliminary experiments and are not included in the results The rabbits were operated on at the age of four to twenty-eight days most of them being six to seven days old at operation

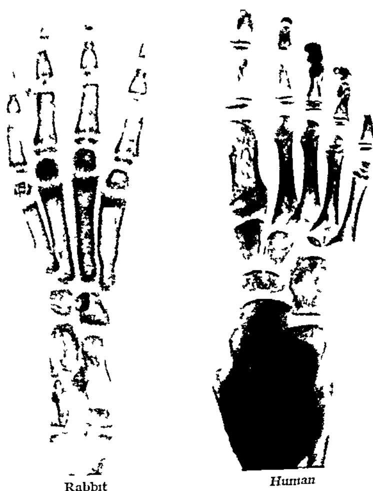


FIG 1 X rays in the dorsoplantar projection of the normal foot of a rabbit and of a man General skeletal structure and relative positions of tarsal bones are strikingly similar The rabbit has four metatarsals and four digits (the first row is missing)

Another method of producing the effect of deformity corresponding to contractures in the periphery was considered The leg muscles including the gastrocnemius and soleus muscles were fixed with nylon thread through a hole bored through the tibia at its halfway point It was expected that the muscles would thus be hampered in growth and normal function with resulting constriction and foot deformity But this too was not wholly successful The muscle evidently either stretched or grew but while attached was able to adapt itself to the growth of the bones so that no true deformities occurred A possible explanation may be found in the tests performed by *Lange* (1929) In a series of experimental rabbits the Achilles tendon and one third to one-half of the belly of the gastrocnemius were excised A silk thread connected the remaining muscle to the calcaneus with approximately normal tension Regeneration of muscle started down the thread in eight weeks and had the appearance of normal muscle and tendon

Tendon fixation or tenodesis was the next method to be tried for provocation of foot deformity The Achilles tendon which is very strong in rabbits as it is in humans could as a rule be fixed successfully to the tibia This fixation maintained the calcaneus in a position of plantar flexion and the Achilles tendon could not adapt itself to the growth of the bones According to *Haines* (1932) a tendon under tension is unable to increase its length But it proved technically impossible to achieve this fully with the very thin and muscular tendons of the tibialis anterior and the extensor digitorum longus at the front of the leg of a rabbit *An attempt was therefore made to cause imbalance of muscle power on this* side by muscle-tendon transections and transection of the ligamentum transversum cruris By this means it was also thought possible to bring about changes in the direction of action of the muscles Observations obtained from paralytic deformities such as those seen in poliomyelitis were considered when planning the experiments But over a year's work on more than 75 rabbits had been done before a method of operation was evolved which brought about a progressive deformity *in the rabbit* resembling the talipes equinovarus deformity *in man* (*Ritsila* 1964)

D TECHNIQUE

1 General operative technique

The operations were performed under aseptic conditions on the left leg under local anaesthesia *(0 75% Xylocain exadrine*)* while the right leg was left intact as a control Longitudinal ventral and dorsal skin incisions

footed plantigrades such as the rabbit; moreover, there is a basic structure of the foot which conspicuously resembles that found in humans. In particular the structure of tarsal bones and their anatomical interrelation are almost similar. The rabbit's foot is admittedly flatter while the metatarsals and toes are comparatively long, and the fore foot has only four metatarsals and digits (Figs. 1 and 2). But the skeletal age at birth and soon afterwards is almost the same in humans and rabbits, as *Heikel* (1960) has noted. Similarities in leg muscles and other soft tissues are also striking, as the study of the anatomy of the rabbit has verified (*Krause* 1884). Hence the young rabbit seems to be a suitable laboratory animal for experiments involving imitation of human foot deformities.

C. DEVELOPMENT OF OPERATIVE METHODS

The initial purpose of the present study was to cause muscular contracture of the leg in rabbits, and thereby to produce foot deformities if possible. This notion had arisen from the quite common clinical observation that in foot deformities in man shortening of muscles and other soft tissue structures appear. The immediate impulse for these experiments was given by shortening of the tibialis posterior muscle and its transformation into a tight string which had often been noted in club foot operations (*Fried* 1959, *Langenskiold* 1961). An attempt was therefore made to produce ischemic contracture by using various methods of blocking the blood circulation. It proved very difficult, however, to produce a permanent contracture in the leg muscles of a growing rabbit, in accordance with earlier studies (*Brooks* 1922). An attempt was also made to produce contracture and fibrosis of the muscles both chemically (by the infiltration of carbolic acid, for instance) and by means of electrocoagulation. No lasting contractures were obtained.

Younger and younger rabbits were taken as test animals as it was noticed that more reliable and lasting changes were produced in young rabbits than in older animals. Lasting changes in four week old rabbits rarely occurred. This is in agreement with the observations of *Crawford* (personal communication to *Wiley* 1959) when he immobilised the feet of a rabbit in dorsiflexion and caused increased resistance to full plantar flexion of the foot by means of resting tension. This myostatic contracture effect was less in adult rabbits than in young ones. For practical reasons the young of rabbits were usually 4—7 days old. Among still younger animals mortality was greater, mainly because of abandonment by the mother.

E METHODS OF INVESTIGATION

1 Radiological study

The deformity and position of the bones were radiologically recorded in all animals The first examination was made one week after operation Radiographs were subsequently taken 3—4 weeks 2 months 3—4 months 6 months and at least 1 year after operation Further radiographs were taken even later if the animal remained alive Finally radiographs of the dissected specimens were taken Dorsoplantar or anteroposterior and lateral projections of both limbs were used

2 Cross section study

Almost all animals were dissected post mortem Specimens were examined by inspection Soft tissue changes deformity and the position of bones were recorded and the degrees of deformity measured from radiographs Photographs of specimens were taken when indicated

3 Histological study

Specimens of eight animals were histologically examined After fixation in neutral formalin and decalcification in ethylene diaminetetra acetic acid the specimens were embedded in paraffin sectioned in the desired planes and stained with haematoxylin *van Gieson*

were made near the ankle (ventral) and Achilles tendon (dorsal) Using normal tendon-stitching technique a nylon thread was sewn to the Achilles tendon The tendon was cut between the *tendinous and muscular* part drawn out and fixed through a hole bored in the middle of the tibia on the medial side so tightly that the talocrural joint was in extreme plantar flexion at the time of the operation On the ventral side transection of the muscles was performed, followed later as a rule by complete *removal of part of the muscle and tendon to eliminate* possible regeneration The same ventral incision enabled transection of the peroneal muscles and of the ligamentum transversum cruris to be performed

2 Plaster of Paris technique

Plaster immobilisation in fixed positions was performed by means of rapidly hardening Cellona® plaster bandage In order to avoid disturbance of blood circulation this was not applied to the whole circumference of the leg The plaster of Paris splint was tied loosely to the limb by gauze bandage As a rule the plaster remained firmly attached to the limb but because of the rabbit s fast growth it had to be changed once a week Like other procedures plaster was applied to the left hind limb leaving the right as a control

3 Fixation technique

With experimental animals on whom other methods of fixation than *a plaster splint were applied in order* to keep the foot in a fixed position the following technique was used By manipulation of the left hind limb the foot was brought into the desired position It was kept there by a nylon thread drawn through the foot between the metatarsals This thread was attached through the tibia halfway along the leg avoiding the *principal nerves and blood vessels* (Fig 3)

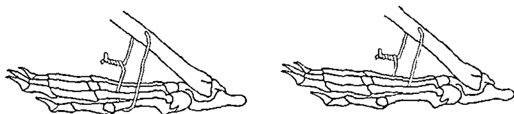


FIG 3 Diagrams to show examples of fixation of the foot of a growing rabbit in a calcaneovalgus position (left) and *in a calcaneovarus* position (right)

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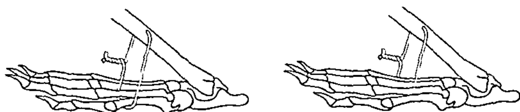


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Specimens of eight animals were histologically examined After fixation in neutral formalin and decalcification in ethylene diaminetetraacetic acid the specimens were embedded in paraffin sectioned in the desired planes and stained with haematoxylin *van Gieson*

F OPERATIONS PERFORMED

The operations were confined to the leg region as fas as possible since operations performed on the foot itself would make estimation of peripheral changes impossible (Fig 15, p 48) Operations on the leg muscles and tendons together with the ligamentum transversum cruris offer an infinite number of possible combinations though not all combinations are adequate for the production of specific effects of muscle imbalance Nineteen different measures were used besides four fixation methods (Table 1)

Table 1 Operative and plaster immobilisation measures with abbreviations taken in experiments with soft tissue components

A_F = Achilles tendon fixation (tenodesis)
A_T = Achilles tendon transection or resection
E_F = extensor digitorum longus muscle or tendon fixation
A_S = Achilles tendon shortening
A → TA = Achillo tibial tenoplasty
A → (E+TA) = Achillo extensoro tibial tenoplasty
E_T = extensor digitorum longus muscle or tendon transection
TA_F = tibialis anterior muscle or tendon fixation
TA_T = tibialis anterior muscle or tendon transection
P_T = transection of all peroneal muscles or tendons
PB_T = peroneus brevis tertius and quartus muscles or tendons transection
PL_T = peroneus longus muscle or tendon transection
TP_F = tibialis posterior muscle (extensor digiti primi) or tendon fixation
TP_T = tibialis posterior muscle (extensor digiti primi) or tendon transection
F_F = flexor digitorum longus muscle or tendon fixation
F_T = flexor digitorum longus muscle or tendon transection
L_T = transection of ligamentum transversum cruris
K_E = plaster of Paris immobilisation in equinus position
K_V = plaster of Paris immobilisation in varus position

Possibilities of combinations of these measures were too great in number for a completely systematic study It was therefore necessary to start from certain hypotheses and continue the choice of combinations on the basis of results in order to achieve specific deformities The next aim was to make a selective search for significant factors in the cases of experimental deformity produced by analysing the dissected specimens The simplest possible combinations for the production of deformity were thus determined Negative results were also important in explaining the factors leading to deformity

A total of 76 operations or other measures including plaster or other fixatio were performed (Table 2)

Table 2 Operations performed and equinovarus and vertical talus deformities

Combination	Number of experiments	Number of equinovarus	Number of vertical talus	Combination	Number of experiments	Number of equinovarus	Number of vertical talus
A_F	4			$A_F+I_T+TA_T+II_T$	2		
L_T	3			$A_F+TA_F+F_T+II_T$	1		
A_F+I_T	13	1	7	$A_F+\Gamma_T+TA_T+P_T$	13		4
$A_F+E_T+I_T$	11		7	$A_F+I_T+TA_T+L_T$	6		
$A_F+TA_T+I_T$	9		6	$A_F+\Gamma_T+\Gamma A_T+\Gamma I_T$	5	2	
$A_F+P_T+I_T$	14		5	$A_F+I_T+TA_\Gamma+TI_F$	1		
$A_F+E_T+P_T$	19	)		$A_F+\Gamma_T+I_T+I_T$	3	1	
$A_F+TA_T+I_T$	23	1	1	$A_F+I_T+I_T+I_T$	3		
$A_F+\Gamma_T+P_T+I_F$	29	11	4	$A_F+\Gamma_T+TA_\Gamma+I_T+ + II_T$	8		
$A_F+\Gamma_I+TA_T$	1						
$A_F+I_T+TI_F$	6			A_T	7		
$A_F+TA_F+P_T$	4			$A_T+\Gamma_T$	1		
A_F+TA_F	10			A_T+TA_T	2		
A_F+L_T	11		3	A_T+TA_F	3		
A_F+TA_T	3			A_T+I_T	3		
A_F+I_T	4			A_T+I_T	5		
$A_F+TA_T+P_T+I_T$	11		7	$A_T+I_T+I_T$	1		
$A_F+I_F+IB_T+I_T$	1			$A_T+\Gamma A_T+I_T$	2		
$A_F+TA_F+I_T$	1			$A_T+TA_\Gamma+I_T$	2		
$A_F+TA_T+I_T$	1			$A_T+\Gamma A_T+I_T$	1		
$A_F+TA_T+P_I$	1			$A_T+TA_I+II_T$	1		
$A_F+TA_F+II_T$	4			$A_T+TA_I+I_T+I_T$	1		
$A_F+I_F+TA_F+II_T$	5						

Table 2 Continued

Combination	Number of experiments	Number of equinovarus	Number of vertical talus	Combination	Number of experiments	Number of equinovarus	Number of vertical talus
A→TA	8			K_E	4		
A→TA $+I_T$	6			K_L+K_V	11	4	
A→TA $+P_T+L_T$	5			$K_F+K_V+I_T$	4		1
A→(F+TA) $+I_T$	4			K_F+I_T	14		3
A_S+P_T	5			$K_F+TA_T+I_T$	2		
$A_S+E_T+P_T$	5			$K_F+I_T+I_T$	2		
$A_S+TA_T+P_T$	4			K_F+P_T	5		
TA_T	1			$K_F+E_T+P_T$	5	2	
PB_T	3			$K_E+K_V+A_T$	3		
TP_F	6			$K_E+K_V+A_T+TA_T+TP_T$	3		
TA_T+P_T	3			Fixation in calcaneo varus position	3		1
TA_T+I_T	8			Fixation in calcaneo valgus position	2		2
TA_T+I_T	1			Fixation in equino varus position	1	1	
F_T+I_T	-			Fixation in equinus position	1		
$E_T+PL_T+I_T$	3			Fixation in equinus $+L_T$	5		
$E_T+PB_T+I_T$	4						
$L_T+P_T+I_T$	4						
				Total	402	32	51

IV RESULTS

A TALIPES EQUINOVARUS

1 *General description of deformity produced and factors leading to deformity*

When the records of the experiments were reviewed it was found that there was a clear regularity in the procedures leading to talipes equinovarus deformity (Table 3) Achilles tenodesis was always performed *producing an equinus position of the calcaneus if it had not been already* produced by plaster immobilisation or other fixation In most rabbits with equinovarus deformity transection of both the extensor digitorum longus muscle and the peroneus muscles had been performed (Table 3)

Table 3 Structural talipes equinovarus deformity in rabbits resulting from various procedures

Series	Rabbit	Operation	Remarks
LVII	No 7	$A_F + L_T$	Good Achilles tenodesis lesion of peroneal nerve extensor and peroneal muscles atrophied
XIII	No 5	$A_T + TA_T + P_T$	Good Achilles tenodesis extensor muscles also atrophied
XXXII	No 6	$A_F + E_T + P_T$	*Good Achilles* tenodesis tibialis anterior and flexor digitorum muscles contracture
XXXII	No 7	— " —	— " —
XXXVIII	No 3	— " —	— " —
— " —	No 4	— " —	— " —
— " —	No 5	— " —	— " —
XLIII	No 3	— " —	— " —
— " —	No 5	— " —	— " —
XLVII	No 3	— " —	— " —
— " —	No 4	— " —	— " —

Table 3 Continued

XXVI	No 10	$A_F+E_T+P_T+L_T$	Good Achilles tenodesis tibialis anterior and flexor digitorum muscles contracture
XXVII	No 4	—•—	—•—
—•—	No 7	—•—	—•—
XXVIII	No 1	—•—	—•—
—•—	No 2	—•—	—•—
—•—	No 3	—•—	—•—
—•—	No 6	—•—	—•—
—•—	No 8	—•—	—•—
XXXII	No 1	—•—	—•—
XLIX	No 1	—•—	—•—
—•—	No 5	—•—	—•—
XXXIII	No 1	$A_F+E_T+P_T+F_T$	Good Achilles tenodesis flexor muscles reattached
XXIV	No 3	$A_F+F_T+TA_T+TP_T$	Good Achilles tenodesis tibialis anterior and tibialis posterior muscles reattached
XXVI	No 5	—•—	—•—
LVIII	No 1	K_E+K_V	Achilles tendon tibialis anterior and flexor digitorum muscles contracture
—•—	No 2	—•—	—•—
—•—	No 7	—•—	—•—
LXI	No 1	—•—	—•—
IX	No 1	$K_E+E_T+P_T$	—•—
—•—	No 4	—•—	—•—
XII	No 7	Fixation in equinovarus position	—•—

Transection of the ligamentum transversum cruris was also performed on several animals developing equinovarus deformity but the deformity also appeared without this measure Severing the ligament clearly accentuated the deforming effect of the tibialis anterior and augmented the adducto-varus position of the metatarsus In some rabbits where the equinovarus position appeared in other combinations careful dissection explained the factors which led to the changes Here too soft tissue changes were in accordance with the deformity and explained its development Thus in Series XIII no 5 in which the combination Achilles tenodesis and transections of the tibialis anterior and peroneal mucles had produced equinovarus it was noted that the extensors were atrophied

while the tibialis anterior had become reattached Muscle-tendon resections had not yet been performed When the test series were renewed using resections this combination did not lead to the equinovarus deformity Similarly in Series XXIV no 3 ($A_T + E_T + TA_T + TP_T$) and Series XXVI no 5 ($A_T + E_T + TA_T + TP_T$) in which muscle tendon resections had not yet been performed but discisions had been extended to include the tibialis anterior and the tibialis posterior it appeared at macroscopic examination that re adherence and contracture had occurred in the region of the tibial muscles In Series XXXIII no 1 where in addition to the combination Achilles tenodesis and transections of the extensor digitorum and peroneal muscles severing of the flexor digitorum had been performed dissection revealed that the flexors had become attached and were tight In Series LVII no 7 with Achilles tenodesis and transection of the ligamentum transversum cruris atrophy of the extensor and peroneal muscles was noted as a possible result of a lesion of the peroneal nerve arising accidentally with Achilles tenodesis

In other animals an equinovarus deformity developed either through external fixation with nylon thread in the equinovarus position (Series XII no 7) or through fixation in the equinovarus position by means of plaster (Series LVIII no 1 etc) But immobilisation must be continued sufficiently long time three weeks at the least Then a permanent even progressive deformity developed

Two interesting experiments are in Series LV nos 1 and 4 Transections of the extensor digitorum and peroneal muscles were performed in connection with immobilisation by plaster in the equinus position producing a typical equinovarus deformity

On the other hand no deformity with equinovarus position developed when resections of the Achilles tendon the tibialis anterior and tibialis posterior muscles were made in connection with plaster immobilisation in the equinovarus position Nor was equinovarus deformity produced in series where one of the factors Achilles tenodesis transections of the extensor digitorum or peroneal muscles was omitted from the combination

Talipes equinovarus deformity was produced in the following combination of three components summarized as follows

First the proximal part of the Achilles tendon was drawn through a hole bored in the middle part of the tibial diaphysis and fixed to the bone Tenodesis was thus performed

Second transection of the peroneal muscles and the extensor digitorum longus muscle was performed A pronator effect was thus eliminated

Third the tibialis anterior the tibialis posterior and flexor digitorum longus muscles with their supinatory effects were left intact

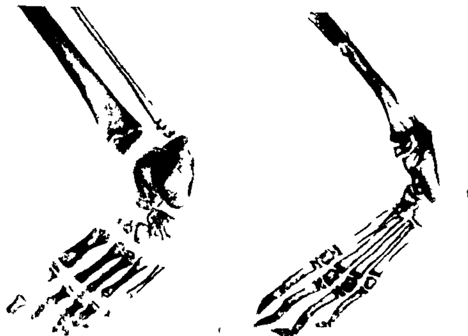


FIG 4 X ray pictures in the dorsoplantar projection of talipes equinovarus of a child (left) and of experimental talipes equinovarus in a rabbit Series XXVIII no 1 (right)

General skeletal structure and relative positions of tarsal bones are strikingly similar

2 Comparison of experimental talipes equinovarus in the rabbit and talipes equinovarus in man

a) General comparison

The deformity known as talipes equinovarus or club foot comprises the following components adduction of the fore foot varus or inversion of the heel and equinus of the entire foot (*Kite* 1964) Club foot also has a cavus deformity (*Ponseti* and *Smoley* 1963)

In all experimental foot deformities noted in Table 3 it was possible to show these different components (Figs 4 and 12)

Clinical examination of the pathology of talipes equinovarus in man is an easy matter since the bones of the foot can be clearly palpated In a club foot the talus is in approximately the same position as in a normal foot that has been strongly adducted an plantar flexed The fore foot and os calcis are medially rotated and displaced around the talus The lateral malleolus is prominent but the medial malleolus is difficult to find by touch Also the head of the talus is prominent on the lateral side of the dorsum pedis The calcaneus is in inversion and equinus deformity

In rabbits with equinovarus deformity the same general changes could be found (Figs 5 and 7)

X ray examination clarifies the position of the bones in the foot and their relationship to one another Comparison of the radiographic appearance of the experimental equinovarus deformity in rabbits with equinovarus deformity in children revealed striking similarities in the dorsoplantar projection it can be seen that the calcaneus has turned into the inversion position under the talus The fore-foot is adducted The navicular cuboid cuneiforms and metatarsals are displaced medially and the fore foot is thus in adduction deformity The navicular is medial to the head of the talus and the cuboid medial to the distal end of the calcaneus (Fig 4)

b) Patho-anatomical comparison of position of bones in relation to each other

The patho anatomical changes in the bones of club-feet were already noted at the end of the 18th century (*Blumenbach* 1786 *Clossius* 1798 *Wantel* 1798 etc according to *Kreuz* 1927) *Antonio Scarpa* in 1803 thought that the deformity was caused by the navicular cuboid and calcaneus moving medial to the talus He observed this while examining club feet in children Renewed study has led to the conclusion that the most notable divergence from normal in the relation of the bones of a club foot apart from the plantar flexed position of the talus is the more medial position of the navicular in relation to the head of the talus (*Kreuz* 1927 *Virchow* 1933 *Wiley* 1959 *Irani* and *Sherman* 1963 *Ponseti* and *Smoley* 1963) *Debrunner* in his monograph suggests that the structure of a club foot is understandable as a twisting of the calcaneus the cuboid the navicular and the whole fore foot into inversion and adduction around the talus *Brockman* (1930) noted that in a club foot there is subluxation of the talocalcaneonavicular joint and alterations in the position of the navicular and calcaneus in relation to the talus The talus is also in the equinus position in the tibio-fibular mortise and it has even been said that a forward subluxation of the talus is present (*Marique* 1946)

When comparing the position of the bones of experimentally produced equinovarus feet with that in a normal foot the changes observed have been very similar to those noted in the literature concerning club foot in man (Figs 6 and 8)

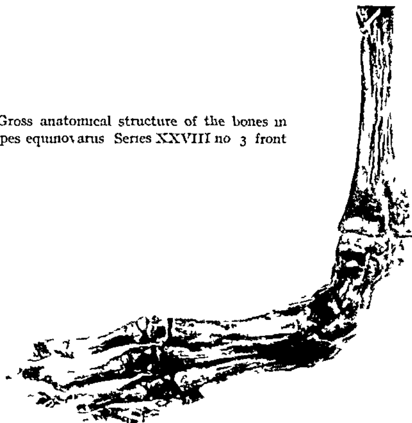
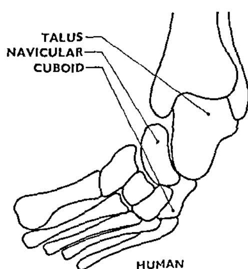


FIG 5 Gross anatomical structure of the bones in rabbit talipes equinovarus Series XXVIII no 3 front view



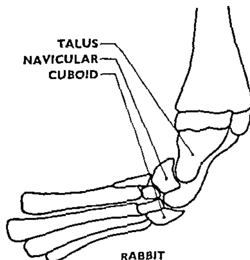


FIG 6 Diagram of Fig 5 compared with diagram of corresponding human talipes equinovarus according to *Kreu.* (1927) (By courtesy of Arch orthop Unfall Chir)
In both the foot is displaced and rotated medially below the talus The head of the talus is on the lateral side of the dorsum of the foot owing to the medial and plantarward displacement of the navicular

FIG 7 Gross anatomical structure of bones in rabbit talipes equinovarus Series XXVIII no 3 rear view

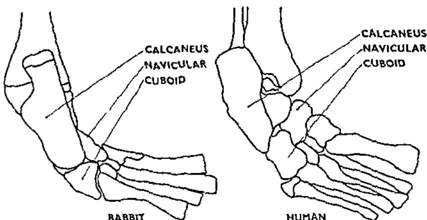


FIG 8 Diagram of Fig 7 compared with diagram of corresponding human talipes equinovarus according to *Kreutz* (1927) (By courtesy of Arch orthop Unfall Chir)

In both the calcaneus is in a severe equinus position with its anterior portion lying below the head of the talus The cuboid is also displaced inward

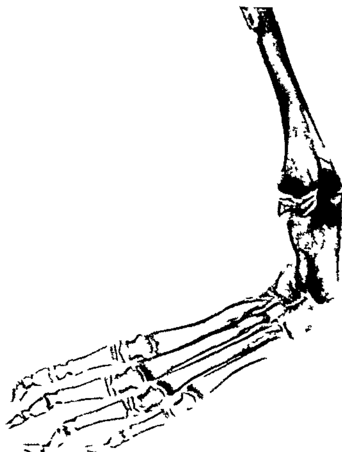


FIG 9 Roentgenogram in the dorsoplantar projection of a rabbit talipes equino varus Series XXXII no 7

c) Radiological comparison of the talo calcaneal angle

X-ray studies add much information about talipes equinovarus to that obtained from clinical examination

The essential difference between a club foot and a normal foot in man is the difference in the angle formed by the longitudinal axes of the talus and the calcaneus According to *Debrunner* (1957) the difference in this angle is so great that a diagnosis can be made on the basis of the roentgenogram alone Small changes in the talo calcaneal angle can be seen on a lateral X ray but the most significant pathology is best seen in the dorsoplantar projection In the normal human foot the talo calcaneal angle in the dorsoplantar projection is a distally open angle of 30—45 degrees according to *Debrunner* and 35—40 degrees according to *Thomasen* (1941) In a club foot the calcaneus is under the talus and the angle between their longitudinal axes the talo-calcaneal angle decreases with the degree of severity Thus in an extreme

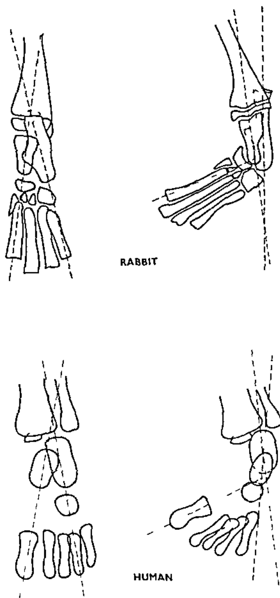


FIG 10 Top diagrams of the dorsoplantar roentgenograms of rabbit s normal foot and club foot Series XXXII no 7 Bottom corresponding diagrams of human feet (*Davis* and *Hart* 1955) (By courtesy of Radiology)

Both in rabbit club foot and human club foot the same radiological changes can be found the talo-calcaneal angle approaches 0 or is reversed the mid talar line lies lateral to the normal position the mid calcaneal line lies medial to the normal position the mid talar line and the line through the shaft of the first metatarsal form an angle

case the axes are parallel or the angle between them may even be reversed (*Davis* and *Hatt* 1955)

It was possible to measure a similar change of angle between the longitudinal axes of the talus and the calcaneus in the dorsoplantar projection in all experimental talipes equinovarus feet (Figs 9 and 10)

d) Comparison of changes in the shape of the talus and the joint surfaces

Descriptions in the literature of bony abnormalities of dissected *infantile club-feet in humans* are in close agreement with each other They suggest that among the changes in the shape of separate bones the most important is the change in the shape of the talus *Adams* (1851–1852) found the greatest changes in the neck and head of the talus The same was noted in later dissection studies (*Kocher* 1878 *Parker* and *Shattock* 1884 *Bissell* 1888 *Bessel-Hagen* 1889 *Burrell* 1893 *Nichols* 1897, *Sheikunenko* 1899 *Bohm* 1929) and described in many other publications (*Mau* 1927 *Kreuz* 1927, *Trues* 1931 *Virchow* 1933 *Debrunner* 1936) *Irani* and *Sherman* in 1963 dissected eleven extremities with equinovarus deformity recovered from stillbirths or from neonatal deaths and constantly found abnormality in the anterior part of the talus In his publication of 1963, *Settle* presented the earlier literature on dissections of infantile congenital talipes equinovarus collected by him He also described his anatomical findings in sixteen dissected infantile club feet In the literature dealing with 52 club feet he noted in 44 cases the same deformity severe distortions of the head and neck as in his own cases *Reimann* (1967) dissected six fetuses stillborns and children with club feet who had died and found almost constantly skeletal changes affecting the talus

The main deformity in the bones of club feet in fetuses was in the neck of the talus which was markedly deviated medially and plantarwards on

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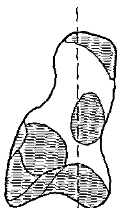
FIG 11 Top the talus of a normal foot (R_n) and of a talipes equinovarus foot (R_t) of the same rabbit Series XXXII no 6 seen from the calcaneal side

Diagrams of these photographs compared with corresponding diagrams of the tali of human normal foot (H_n) and club foot (H_t) from the late fetal period according to *Settle* (1963) (By courtesy of J Bone Jt Surg)

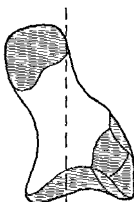
Similarities between the normal talus and the talus of club foot in both human and rabbit are marked the tali of club feet have an obvious medial rotation of the neck the articular surface towards the navicular is displaced medially and plantarward *in club feet* the anterior articular surface towards the calcaneus is missing

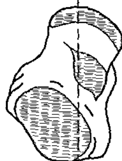






RABBIT





HUMAN

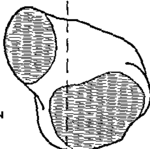


Fig 11

case the axes are parallel or the angle between them may even be reversed (*Davis* and *Hatt* 1955)

It was possible to measure a similar change of angle between the longitudinal axes of the talus and the calcaneus in the dorsoplantar projection in all experimental talipes equinovarus feet (Figs 9 and 10)

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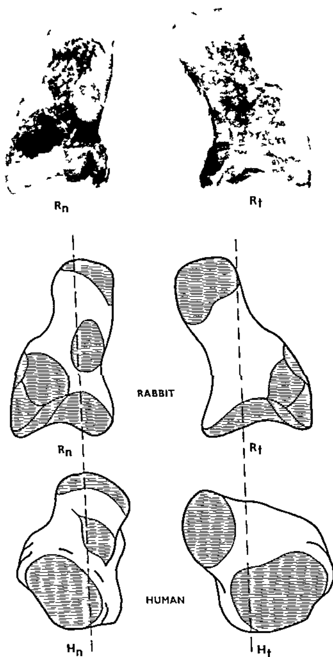


Fig 11

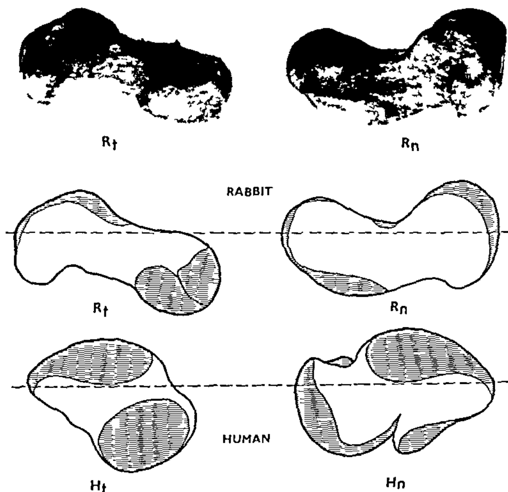


FIG 1 Top the medial side of the tali of a rabbit left from a club footed specimen (R_t) right from a normal one (R_n) Series XXXII no 6

The centre pictures are diagrams of these tali

The bottom illustrations are corresponding diagrams of tali in human congenital equinovarus foot (H_t) and in human normal foot (H_n) (*Settle* 1963) (By courtesy of J Bone Jt Surg)

In this direction the similarities between the normal talus and the talus of club foot in both human and rabbit are also obvious both tali of human and rabbit club foot have the same kind of plantar deviation of the neck and medial displacement of the articular surface towards the navicular

the body of the talus The angle between the long axis of the neck and the long axis of the body of the normal talus is 150—155 degrees while in a club foot it is 115—135 degrees (*Irani* and *Sherman* 1963) Upon the deformed and deviated neck of the talus the talo navicular articular surface displaces still further medially and plantarwards increasing the deformity even more The subtalar articular surfaces fuse together in a

single distorted articular surface which faces medially in internal rotation and equinus (*Settle* 1963)

The same pathological changes as in the talus of an infantile club foot have also been noted in these macro-anatomical studies of experimental club foot in rabbits The degree of deformity in the talus was directly proportional to the degree of equinovarus deformity The more extreme the equinovarus position the greater the medial deviation of the neck of the talus and the medial displacement of the talo navicular articular surface (Figs 11 and 12)

The navicular in experimental equinovarus feet is regularly smaller than in a normal foot in the same rabbit This has also been noted in fetal club feet (*Irani* and *Sherman* 1963 *Settle* 1963)

Changes in the shape of other bones and articular surfaces of club-feet in both humans and rabbits are smaller The calcaneus and cuboid remain almost normal as the literature has suggested (*Irani* and *Sherman* 1963 *Settle* 1963) In extreme experimental equinovarus feet however these bones show greater changes corresponding to the deformity

e) Comparison of changes in soft tissues

There are very few good anatomical studies on soft tissue changes in club-foot deformity Clinical observations and those made during operations on club-feet are numerous but they are partial and separate observations and do not cover all the factors having an effect in these cases Earlier authors mainly clarified the bone changes and not until recent decades have soft tissue changes received the attention they deserve However *Little* (1839) had already shown that uncoordinated muscle function or abnormal tendon insertions could cause club foot deformity Most investigators have studied tendon insertions and found anomalies in them (*Scherb* 1930 *Penners* 1954) *Debrunner* (1957) wrote that these anomalies have been found in almost all the tendons of club feet

A general observation in talipes equinovarus specimens in rabbits produced both by means of Achilles tenodesis and by plaster and fixation immobilisation was the displacement of the Achilles tendon insertion to the medial side of the tuber calcanei On the other hand the calcaneus in relation to the talus rotates into inversion and thus it is difficult to say whether it is a displacement of the tendon insertion or a displacement of the bone in relation to the tendon A similar Achilles tendon displacement has however been observed in many examinations

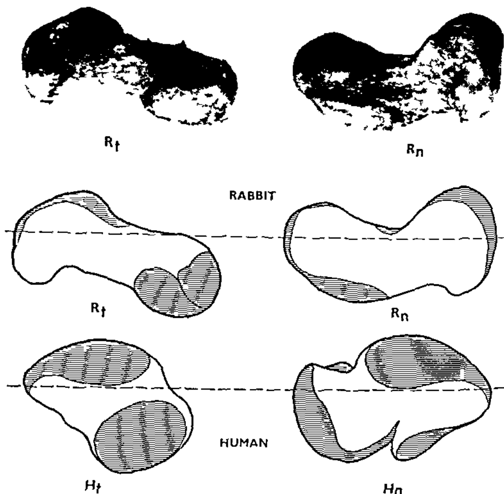


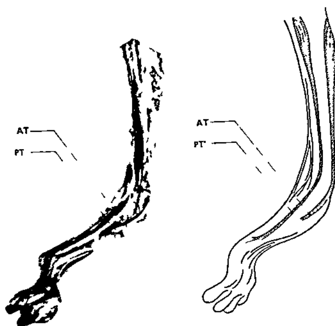
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The centre pictures are diagrams of these tali

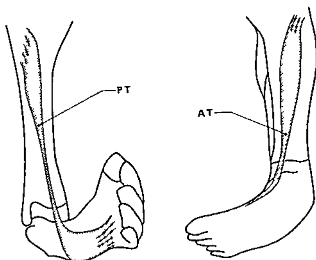
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the body of the talus The angle between the long axis of the neck and the long axis of the body of the normal talus is 150—155 degrees while in a club foot it is 115—135 degrees (*Irani* and *Sherman* 1963) Upon the deformed and deviated neck of the talus the talo navicular articular surface displaces still further medially and plantarwards increasing the deformity even more The subtalar articular surfaces fuse together in a



RABBIT
Medial view



HUMAN

Fig 13

of club foot in man (*Flinchum* 1953 *Penners* 1954 *Inclan* 1958) In his studies *Stewart* (1951) frequently found this tendon insertion anomaly which strengthens the supinating effect of the Achilles tendon

When analyzing the gross talipes equinovarus specimens in rabbits it was always noticeable that supinating muscle tendon structures the Achilles tendon the tibialis anterior and tibialis posterior muscles and the flexor digitorum muscles were shortened and taut compared with the normal foot of the same rabbit These changes occurred in experimental deformities produced by Achilles tenodesis and by transection of the peroneal muscles and the flexor digitorum longus muscles or in club foot deformities produced by immobilisation into the equinovarus position In club foot in man the Achilles tendon contracture is a constant phenomenon From his investigations *Stewart* draws the conclusion that the triceps surae muscle the tibialis anterior muscle and the short plantar muscles are positively deforming forces while the peroneal muscles are insufficient and do not prevent the foot from turning towards equinovarus deformity Other authors have also placed emphasis on either the contracture or fibrosis and shortening of the tibialis posterior muscle (*Mau* 1930 *Fried* 1959) or the abnormal resistance to eversion of the tibialis anterior muscle (*Flinchum* 1953) Recently *Attenborough* (1966) has confirmed the finding of small muscle bellies and shortness of the gastrocnemius soleus tibialis posterior and flexor digitorum longus muscles in stillborn infants with club feet

In the experimental talipes equinovarus specimens it has been possible to observe similar shortening and contractural tightening of the Achilles tendon the tibialis anterior and posterior muscles and the flexor digitorum longus muscles as described in the literature (Fig 13)

FIG 13 Top left a picture of a rabbit club foot Series LVIII no 7 top right a diagram of the same picture

Bottom illustrations taken from the literature showing human fetal club foot specimens Bottom left club foot of an eight month old fetus showing the tightened and shortened tendon of the tibialis posterior (PT) muscle and its longer tendinous part (*Mau* 1930) (By courtesy of Arch orthop Unfall Chir)

Bottom right a club foot of a six and a half month old fetus showing the same change in the tibialis anterior muscle (AT) (*Flinchum* 1953) (By courtesy of J Bone Jt Surg)

Experimentally the same changes in the supinator and adductor muscles the tibialis anterior (AT) the extensor digiti primi (PT) (in rabbit homologous perhaps to the tibialis posterior in man) and the flexor digitorum longus could also be found in all club foot specimens These muscles offered abnormal resistance of eversion

CORRECTIONS

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f) *Micro anatomical comparison*

Bernbeck (1954) has presented micro-anatomical studies on talipes equinovarus specimens of fetuses in which a marked bone deformity was clearly seen The greatest change was in the talonavicular joint where the navicular had shifted medially and plantarward around the talus The fore-foot and cuboid also shifted with the navicular

In all three micro anatomical studies of vertical sections of experimental talipes equinovarus deformities in rabbits a similar striking bone change could be found (Fig 14)

In these experiments on rabbits as well as in *Bernbeck* s studies molding of the head of the talus and the navicular can also be seen The neck of the talus has deviated medially the navicular articulation with the talus has an inclination towards the medial surface of the foot and the talonavicular and the calcaneocuboid joints have turned medially

FIG 14 Top left a micro anatomical section in the frontal plane of a club foot in fetus (*Bernbeck* 1954—1955) (By courtesy of Ferdinand Enke Verlag Stuttgart)

Top right the same section of a club foot of a rabbit Series XXVIII no 1

Bottom corresponding diagrams

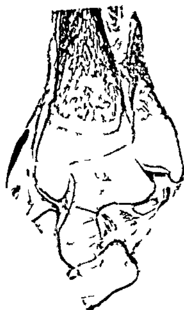
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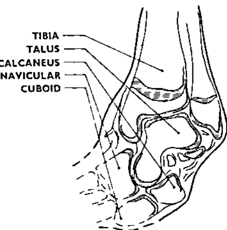
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HUMAN



RABBIT



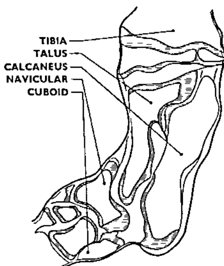


Fig 14

Table 4 Continued

Series	Rabbit	Operation	Remarks
XLIX	No 4	$A_F+T_T+P_T+L_T$	Good Achilles tenodesis tibialis anterior muscle contracture
XLIV	No 1	$A_F+TA_T+P_T$	Good Achilles tenodesis extensor muscle attached
LIX	No 4	A_F+E_T	Good Achilles tenodesis tibialis anterior muscle attached
—"—	No 5	—"—	—"—
—"—	No 6	—"—	—"—
XXIX	No 1	$A_F+TA_T+P_T+L_T$	Good Achilles tenodesis extensor digitorum muscle contracture
XXIX	No 2	—"—	—"—
—"—	No 3	—"—	—"—
XLI	No 6	—"—	—"—
—"—	No 7	—"—	—"—
LI	No 2	—"—	—"—
—"—	No 2	—"—	—"—
XXIII	No 1	$A_F+E_T+TA_T+L_T$	Good Achilles tenodesis not resections but discisions dorsiflexor muscles reattached
—"—	No 2	—"—	—"—
—"—	No 3	—"—	—"—
—"—	No [illegible]	—"—	—"—
LVIII	No 6	$K_L+K_X+I_T$	Achilles tendon and dorsiflexor muscles contracture
LXI	No 2	K_E+I_T	—"—
—"—	No 3	—"—	—"—
LXIV	No 2	—"—	—"—
XII	No 3	Fixation in calcaneovarus position	—"—
—"—	No 4	Fixation in calcaneovalgus position	—"—
—"—	No 5	—"—	—"—

Macroscopic analysis of the vertical talus specimens thus obtained led to the conclusion that sufficiently tight fixation of the Achilles tendon to the tibia causes the calcaneus to turn downwards in plantar flexion At the same time it is clear that the talus also turns more vertically

Severing of the ligamentum transversum cruris causes the tibialis anterior and extensor digitorum longus muscles to become in ufficient at first but later they shorten and begin to tighten (Fig 15 p 48) In addition *the tendons of the extensor digitorum longus adhere to the dorsum pedis and the muscle effect is transferred from the toes to the tarsus* Similarly the pull of the tibialis anterior muscle is exerted more directly towards the insertion point at the base of the first metatarsal In operations on several children with vertical talus deformity at the Orthopaedic Hospital of the Invalid Foundation it was noted that the tendons of the extensor digitorum longus in these cases adhered to the dorsum pedis in the same way (*Langenskiold* 1964) thus causing a transference of muscular pulling effect from the toes to the forepart of the tarsus as in the rabbits with the experimentally produced deformity

Vertical talus deformity also developed *when either the extensor digitorum longus or the tibialis anterior muscles were resected in addition to sectioning of the ligamentum transversum cruris and fixation of the Achilles tendon* The two forms of vertical talus thus obtained differ from each other If the tibialis anterior is resected a deformity arises with dorsiflexion pronation and abduction in the distal part of the foot (Fig 20 p 55) the changes occurring mainly at the mid tarsal joint If in turn the extensor digitorum longus muscles are resected a slight supination towards dorsiflexion in the distal part of the foot and a tendency to varus position are provoked (Fig 18 p 54) Vertical talus deformity produced merely by discision of the ligamentum transversum cruris and fixation of the Achilles tendon are predominantly of the first type the extensor digitorum longus and the peroneal muscles strength overcoming the effect of the tibialis anterior When the children with *vertical talus* deformity seen at the Orthopaedic Hospital of the Invalid Foundation were examined it was possible to distinguish both these vertical talus deformity types (*Langenskiold* 1964)

In the so-called tibialis anterior type (Figs 17 and 18 p 54) the tibialis anterior tendon is a tightened and shortened element on the anterior side of the ankle while in the so-called extensor digitorum type (Figs 19 and 20 p 55) the extensor tendons and the peroneal tendons are contracturally tightened and shortened

It is a fact of great interest that when tension of the Achilles tendon which is produced by evident myostatic contracture of the gastrocnemius and soleus muscles secondary to plaster immobilisation alone was combined with a myostatic dorsiflexion contracture produced by transection of the ligamentum transversum cruris a vertical talus deformity also developed (Fig 16)



FIG 16 Vertical talus deformity in a rabbit Series LXI no 3 produced by plaster immobilisation and transection of the ligamentum transversum cruris The sole is convex the calcaneus is in the equinus position the fore foot is in dorsiflexion and the talus is in a clearly vertical position

2 Comparison of experimental vertical talus in the rabbit with vertical talus in man

a) General comparison

Though the clinical picture should cause suspicion of the vertical talus deformity it is the radiograph which is characteristic Therefore the general comparison of both the tibialis anterior and the extensor digitorum types in children and rabbits is presented by means of X ray pictures

In the lateral projection in both types in rabbits and in man the sole is convex the forepart of the foot is in dorsiflexion and the talus points downwards into the sole of the foot The calcaneus is carried into the equinus position with the talus The navicular does not articulate with the head of the talus but faces the dorsal surface of its neck (Figs *17 and 19*)

In the anteroposterior projection the tibialis anterior type has a slight supination of the forepart of the foot while the extensor digitorum type has clear pronation (Figs 18 and 20)

There are remarkable similarities in the general shape of the bones and the relative positions of separate bones in children and in rabbits

FIG 17 Lateral roentgenogram of a vertical talus the tibialis anterior type Top deformity in a child bottom in a rabbit Series LII no 1

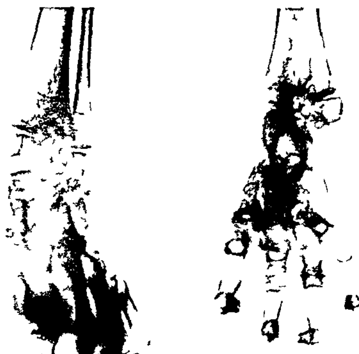
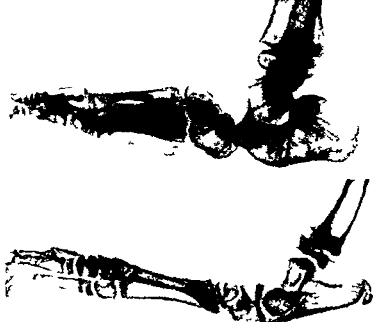
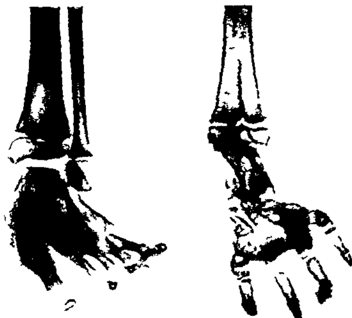


FIG 18 *Anteroposterior roentgenogram* of the same vertical talus deformity in a child and in a rabbit as in Fig 17



I I(1) Lateral roentgenogram of a vertical talus the extensor digitorum type Top deformity in a child bottom in a rabbit Series I no 1



I I(o Anteroposterior roentgenogram of the same vertical talus deformity in a child and in a rabbit as in Fig 1)

b) Patho-anatomical comparison of the position of bones in relation to each other

There are few investigations dealing with the gross anatomical changes in the vertical talus deformity Usually only the clinical and radiological characteristics of the deformity have been described The only detailed description from earlier times is according to *Guntz* (1939) that of *Kustner* (1880) It was not until 1939 that *Guntz* carefully examined the pathology of the congenital flat-foot deformity by dissecting the deformed feet of a stillborn child He found the same bone changes as *Kustner* In 1963 *Herndon* and *Heyman* presented illustrations of the pathological anatomy of the congenital convex pes valgus as they term the congenital vertical talus A complete patho anatomical study of a six week old infant with bilateral congenital convex pes valgus has been published very recently (*Patterson Fitz* and *Smith* 1968)

According to earlier examinations, the downward rotation of the talus into a vertical position and subluxation of the navicular which articulates with the dorsal aspect of the neck of the talus locking it in a plantar flexed position are essentials in the bone relationships of congenital flat-foot or congenital convex pes valgus deformity

In all rabbits with vertical talus it was exactly this relationship of the talus and the navicular that was very obvious It was very difficult during dissection to separate the talus and to turn it from the vertical position without breaking the bones because the talus was locked in a plantar flexed position by the navicular (Fig 21)

From the dorsal aspect it was essential that the head of the talus was directed medially and inferiorly with the result that the axis of the talus deviated more medially than normally (Figs 22 and 23)



I IC - Patho anatomical pictures of the dorsal aspect of vertical talus deformity (left) and (right) normal foot in a rabbit Series XL no - Tibia has been removed In vertical talus deformity the long axis of the talus deviates medially and the neck has been turned medially and plantarward

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I IC -3 Top diagrams I - Bottom corresponding illustrations of human Knickplattfuss according Niederecker (1 50) (By courtesy of Z Orthop) In both human and rabbit there is a similar medial deviation of the long axi of the talus in the deformed foot

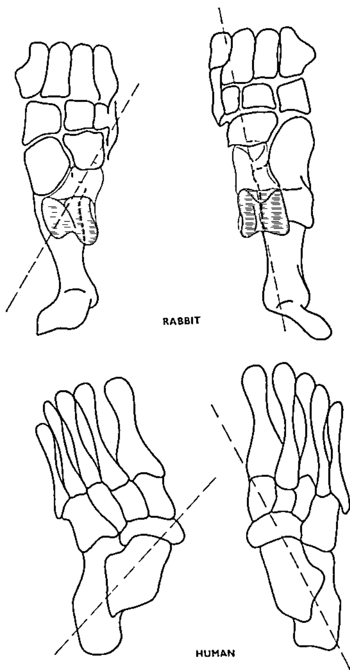
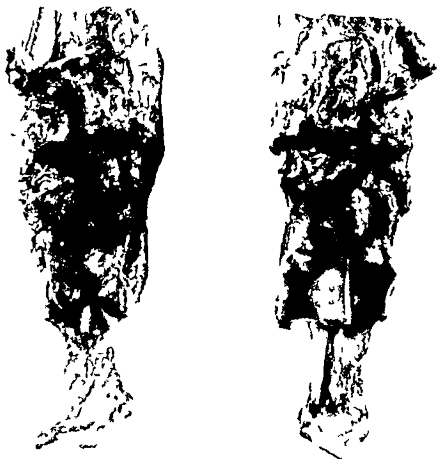


Fig 23

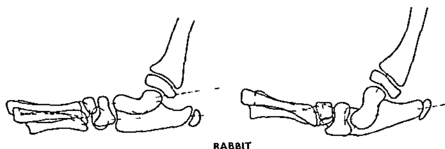


I I(2 I atho anatomic il pictures of the dorsal aspect of vertical talus de formity (left) and (right) normal foot in a rabbit Series XI no 2 Tibia has been removed In vertical talus deformity the long axis of the talus deviates medially and the neck has been turned medially and plantarward

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I IG 23 Top diagrams I ig Bottom corresponding illustrations of human Knickplattfuss ac or ling sиederecker (1 150) (By courtesy of Z Orthop)
In both human an l i a t it there is a similar medial deviation of the long axis of the talus in tl le formed foot





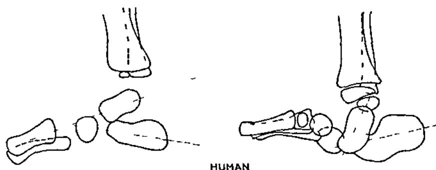


FIG. 24 Top lateral roentgenogram of a vertical talus foot in a rabbit Series I no 1

Centre right diagram of the same foot centre left diagram of the rabbit normal foot

Bottom right diagram of human congenital flat foot bottom left diagram of human normal foot from a publication by *Davis* and *Hall* (1955) (By courtesy of Radiology)

The diagrams show an increased talo-calcaneal angle in the deformed feet on the lateral projection both in man and rabbit

c) Radiological comparison of the talo-calcaneal angle

In order to estimate and compare the X ray examinations of the foot objectively, it is necessary to draw axes of the bones and to measure the angles formed by them Changes in the angle formed by the longitudinal axes of the talus and the calcaneus (the talo calcaneal angle) are characteristic of the congenital vertical talus and also of the congenital club foot *Guntz* (1939) has made a thorough radiological comparison of various foot deformities He has found that the talo calcaneal angle both in lateral and dorsoplantar projections in all flat foot deformities is wider than normal *Huner* (according to *Niederecker* 1959) has measured the talo calcaneal angle in the lateral projection of the normal foot at a minimum of 20 degrees while it can be 90 degrees in congenital flat-foot *Siegmund* reported (according to *Hohmann* 1951) the talo calcaneal angle in the lateral projection to be 50—90 degrees in congenital flat foot and 28 degrees in normals

Radiographs taken in the dorsoplantar projection reveal medial displacement of the distal part of the talus This radiographic finding is similarly described by *Osmond Clarke* (1956) *Lloyd Roberts* and *Spence* (1958) *Harveson* (1959) *Outland* and *Sherk* (1960) *Herndon* and *Heyman* (1963) Apart from *Guntz* other German authors have also observed the increase in the talo calcaneal angle in the dorsoplantar projection According to *Hohmann* the talus in congenital flat-foot can be directed transversally to the calcaneus which is in the direction of the longitudinal axis of the foot In clinical material *Huner* has found the talo calcaneal angle in the dorsoplantar projection to be about 20 degrees in normals but much wider in congenital flat foot up to 45 degrees On the other hand *Storen* (1967) claims that the talo-calcaneal angle is reduced in the dorsoplantar projection in congenital convex pes valgus with vertical talus but not in all cases

In rabbits with vertical talus an increase in the talo calcaneal angle both in the lateral and the dorsoplantar projection in comparison with the normal foot could be found (Figs 24 25 and 26)

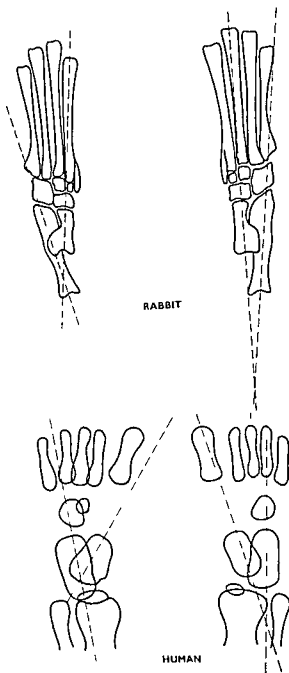


Fig 26

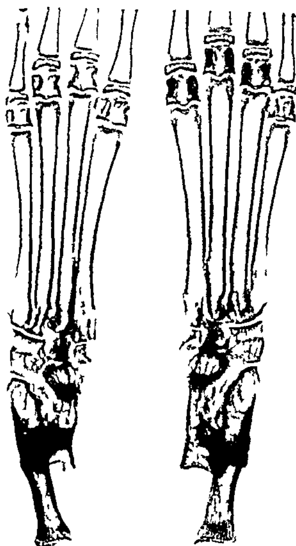


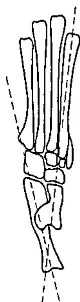
FIG. 25. Left: dorsoplantar roentgenogram of a vertical talus foot in a rabbit of the 'tibialis anterior' type, Series III no. 2. Right: the normal foot of the same rabbit.

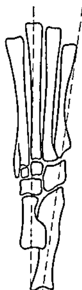
FIG. 26. Top: diagrams of Fig. 25.

Bottom: corresponding illustration of a congenital flat foot in man (left) and a normal foot (right) from a publication by *Davis* and *Hall* (1955).

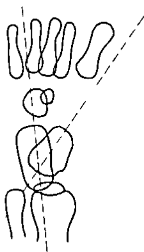
(By courtesy of Radiology.)

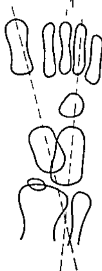
The diagrams show an increased talo-calcaneal angle in the deformed foot in the dorsoplantar projection both in man and rabbit.





RABBIT





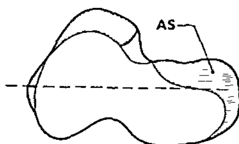
HUMAN

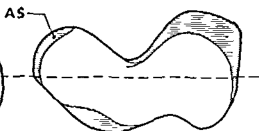
Fig. 26





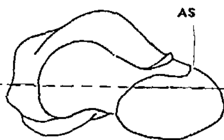
RABBIT

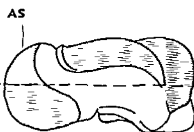




vertical talus

normal





HUMAN

FIG 28 Top medial view of the tali of the vertical talus foot and normal foot in the same rabbit Series XI no 4

Diagrams of these photographs compared with corresponding diagrams of the tali of human vertical talus and normal foot from a publication by *Patterson Fitz* and *Smith* (1968) (By courtesy of J Bone Jt Surg)

The shaded areas are articular surfaces AS = articular surface of the talo navicular joint In this projection the similarities between the human and rabbit deformed tali are obvious the talonavicular joint surface is medially displaced and the caput tali is deformed

e) Comparison of changes in soft tissues

In order to clarify possible deforming factors in experimentally produced vertical talus deformity muscle and tendon structures were examined macroscopically It was found that the equinus position of the hindpart of the foot and the Achilles tendon contracture or shortening could be developed either by Achilles tenodesis or by plaster or external fixation of the os calcis in the equinus position

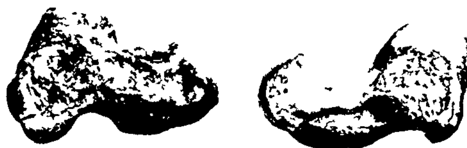
Many earlier investigators have observed the Achilles tendon shortening or contracture in vertical talus deformity in children (*Harreson* 1959 *Herndon* and *Heyman* 1963 *Patterson Fitz* and *Smith* 1968) Many authors have also suggested an elongation of the tightened Achilles tendon in operative reduction of the congenital vertical talus deformity (*Rocher* and *Pouyanne* 1934 *Hark* 1950 *Hohmann* 1951 *Outland* and *Sherk* 1960 *Mead* and *Anast* 1961)

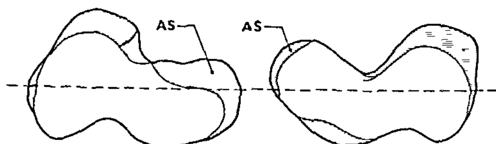
According to *Gunt* s patho-anatomical examination of the vertical talus deformity the Achilles tension did not seem to be noteable in the deformed position but when the lateral dislocation of the calcaneus was reducted to the normal position the Achilles tendon had to be tenotomized because the lateral fibres tightened and thus prevented reduction

In one group of rabbits with experimental vertical talus deformity tension of extensor and peroneal tendons caused a dorsiflexion position of the fore foot This was called the extensor digitorum type In most cases described in the literature the dorsiflexion contracture has been observed in precisely the extensor digitorum longus and peroneal tendons (*Mead* and *Anast* 1961 *Herndon* and *Heyman* 1963) and many authors found that a transection of the tibialis anterior tendon was not indicated or proved useful if performed (*Osmond Clarke* 1956 *Lloyd Roberts* and *Spence* 1958 *Herndon* and *Heyman* 1963)

In another group of rabbits with vertical talus deformity tibialis anterior and extensor digitorum longus tendon tension could be found The literature also contains reports of similar contractures in the vertical talus deformity in man (*Hark* 1950 *Outland* and *Sherk* 1960 *Patterson Fit* and *Smith* 1968)

In the third group of rabbits with vertical talus deformity the essential dorsiflexion contracture was found in the tibialis anterior tendon This group was called the tibialis anterior type *Hughes* (1957) has stated that in the congenital vertical talus in man there are also contractures of the anterior soft parts particularly the tibialis anterior muscle However German writers in particular have put emphasis on





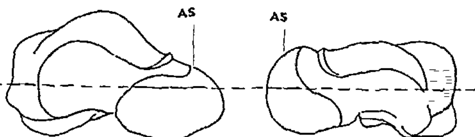


FIG 28 Top medial view of the tali of the vertical talus foot and normal foot in the same rabbit Series XI no 4

Diagrams of these photographs compared with corresponding diagrams of the tali of human vertical talus and normal foot from a publication by *Patterson Fitz* and *Smith* (1968) (By courtesy of J Bone Jt Surg)

The shaded areas are articular surfaces AS = articular surface of the talo navicular joint In this projection the similarities between the human and rabbit deformed tali are obvious the talonavicular joint surface is medially displaced and the caput tali is deformed

RABBIT

HUMAN

FIG 23 Top rabbit vertical talus foot specimen Series LVII no 8 Centre diagram of the same picture

Bottom corresponding diagram of human Knickplattfuss from a publication by Ni derecker (1950) (By courtesy of Z Orthop)

Both in rabbit and man a similar bowstringing and displacement of the effect of the tibialis anterior tendon more anteriorly can be found.

the tibialis anterior contracture as a deforming factor in "der angeborene Knickplattfuss" as they term the congenital vertical talus *Guntz* (1939) made an exact patho anatomical study of the congenital flat foot and found the tibialis anterior tendon a factor that hindered the plantar flexion of the fore foot It tightened like a string from the leg to the dorsum of the foot at the same time as the ligamentum cruciatum cruris had moved more proximally fusing with the ligamentum transversum cruris (Fig 29) According to *Guntz* the extensor digitorum longus tendons also tighten strongly in the plantarflexion position of the fore foot On the basis of extensive material consisting of operated flat feet *Niederecker* (1950) emphasized that functional factors or muscle anomalies are more important than bone factors He considered that the hypertrophy and contracture of the tibialis anterior muscle strengthened the development of the flat foot deformity He also noted that the insertion of the tibialis anterior tendon very significant in flat foot deformity had moved forwards to the first metatarsal bone *Patterson Fitz* and *Smith* (1968) described also the bowstringing of the anterior tibial tendon (Fig 29)

In rabbits in which the peroneal muscles were preserved contractural shortening could be observed especially in the extensor digitorum type *Guntz* (1939) has referred to the contracture of the peroneus brevis muscle and its deforming effect in man *Herndon* and *Heyman* (1963) have also noticed the contracture of both peroneal muscles During the operative reduction of the congenital vertical talus feet of children at the Orthopaedic Hospital of the Invalid Foundation the peroneus tertius muscle and its contracture and deforming effect have often been found (*Langenskiold* 1964) *Niederecker* (1950) has also observed the occurrence and the importance of this muscle in flat foot deformity

But even if the muscle and tendon contractures in vertical talus experiments were released it was not possible to correct the deformity and the position of the talus until the ligamentous contractures were released In rabbits it was found that the most important factors that hindered the correction of the vertical talus deformity were the talo navicular ligament the talocalcaneal interosseum ligament and especially the tibionavicular ligament Many authors have paid attention to the significance of these ligamentous factors in the congenital vertical talus deformity during the operative reduction of this deformity (*Hark* 1950 *Osmond Clarke* 1956 *Mead* and *Inast* 1961 *Herndon* and *Heyman* 1963 *Storen* 1967)

V DISCUSSION AND CONCLUSIONS

The purpose of the studies described above was not to determine the unexplained primary etiology of congenital deformities of the foot but to analyse the part played by muscle imbalance and by soft tissue factors generally in the pathogenesis of structural bone deformities of the foot. The aim was also to produce in the growing rabbit by measures performed on soft tissues and through muscle imbalance and contracture experimental changes which resemble foot deformities seen in humans.

Therefore only the muscle and other soft tissue contractures related to human foot deformities and to animal experiments are discussed. In addition only the points in common which could be noted when comparing the morphological, radiological, patho-anatomical and especially soft tissue changes of talipes equinovarus and vertical talus produced in rabbits with these deformities in man are discussed. Conclusions have been made on the same bases.

A MUSCLE IMBALANCE AND SOFT TISSUE CONTRACTURES RELATED TO CONGENITAL FOOT DEFORMITIES IN MAN AND TO ANIMAL EXPERIMENTS

In connection with paralytic deformities which include both traumatic deformities and those following poliomyelitis many observations were made of bone changes arising from changes in the soft tissues. In poliomyelitis for instance where imbalance of muscle power is the cause of deformity restoration of muscle imbalance when effected sufficiently early by appropriate transposition of tendons has often prevented the development of a seriously progressive deformity such as talipes calcaneus or varus and especially its transformation into a structural bone deformity. In addition much information on patho-anatomical soft tissue changes in congenital deformities especially club-foot has been obtained. The old static conception of bone deformity as a primary condition is yielding to more dynamic thinking although studies still appear which place bone deformity in the foreground (*Thomasen* 1941 *Doyle*

f) Micro anatomical comparison

Five vertical talus specimens of rabbits were sectioned and examined histologically in the sagittal plane through the talo-navicular joint

The following similar phenomena in the sagittal plane of both the vertical talus experiments in rabbits and the vertical talus deformity in an infant can be seen in the illustrations (Fig 30) The navicular has an abnormal articulation with the superior surface of the neck of the talus, the talus rotates toward the plantar surface into a vertical position and the deformed appearance of the head of the talus is demonstrated here as in Fig 28

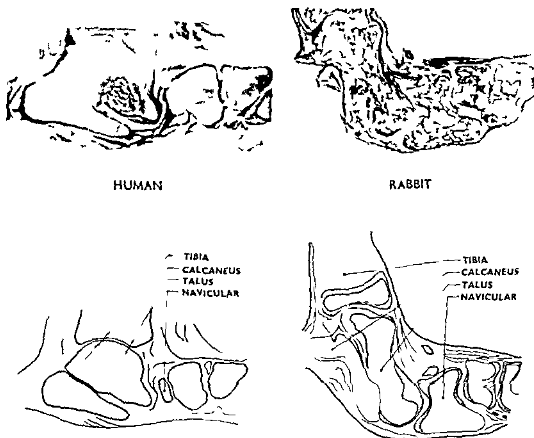


FIG 30 Top left a micro anatomical section in the sagittal plane of a vertical talus in an infant (*Patterson Fitz* and *Smith* 1968) (By courtesy of J Bone Jt Surg)

Top right the same section of a vertical talus in a rabbit Series XL no 1

Bottom corresponding diagrams

See text above

V DISCUSSION AND CONCLUSIONS

The purpose of the studies described above was not to determine the unexplained primary etiology of congenital deformities of the foot but to analyse the part played by muscle imbalance and by soft tissue factors generally in the pathogenesis of structural bone deformities of the foot The aim was also to produce in the growing rabbit by measures performed on soft tissues and through muscle imbalance and contracture experimental changes which resemble foot deformities seen in humans

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1961; *Irani* and *Sherman* 1963). An increasing number of recent investigators have directed their attention to soft tissue anomalies in congenital and idiopathic deformities (*Scherb* 1930, *Stewart* 1951, *Flinchum* 1953, *Langenskiöld* and *Michelsson* 1961). *Debrunner* (1957), for instance, has suggested that an essential feature of club foot is active contracture of the soft tissues caused by disturbed muscle balance.

Close investigation of bone changes in various congenital foot deformities has led to greater uniformity, but observations on soft tissue changes vary. Although contractural changes in them are often observed, the microscopic findings themselves are variable. This is in agreement with the statement of *Ferguson, Vaughan* and *Ward* (1957) that histological changes in muscle are notoriously difficult to evalute and disagreement as to the presence or absence of histological changes runs throughout the literature on disuse atrophy and myostatic contracture. The only difference microscopically between the muscles in club foot deformity and those of a normal foot is that in the former atrophied muscle fibres are found between normal ones (*Mau* 1930) or the average diameter of the muscle fibres is diminished (*Reimann* 1967). This is most noticeable in supinatory muscles. But a similar discovery has been made in poliomyelitis, that is in muscles which have changed through disturbance of the central nervous system, and also in ischemic contractural muscles (*Debrunner* 1957). Thus *Debrunner* has said that congenital club foot is the brother of paralytic club foot.

As soft tissue contracture is a conspicuous feature of congenital foot deformity, at least in its later stages, the attempt to produce muscle contracture in the leg of a growing rabbit and thus possibly to imitate congenital foot deformities was of interest. Ischemic contracture seemed suitable for this purpose, but permanent contracture was not obtained by this means. Why was ischemic contracture difficult to achieve? As *Brooks* (1922) has shown in his experimental studies, blockage of the arterial blood circulation of muscles causes either complete necrosis and destruction of the muscle if collateral circulation is insufficient, or preservation of the muscle with normal appearance and functioning if collateral circulation is sufficient. Arterial production of ischemic contracture does not succeed; in fact, fibrosis and shortening of the muscle do not occur. *Brooks* states, however, that obstruction of the purely venous blood circulation does cause fibrosis and muscle shortening and that extravasation of the red corpuscles and disturbed nutrition of tissues cause changes. In the present tests the production of disturbance in the purely venous blood circulation of rabbit muscles was hardly

successful *Clark* (1946) has shown moreover that endomysium remaining after partial experimental ischemic necrosis has astonishing ability to regenerate the endomysial tubes It is thus understandable that attempts to produce permanent ischemic muscle contracture were unsuccessful

Soft tissue contracture which develops during plaster immobilisation is a well known clinical phenomenon Also experimental studies described in the last century produced contractures in striated muscles when they were kept shortened for a certain time by methods including moving the muscle s points of attachment nearer to the origin (*Moll* 1886) or severing the muscle tendon to make the muscle contract A fixation of the muscle then occurs at the length imposed upon it This contracture is called myostatic though its pathogenesis has not been fully explained If immobilisation is interrupted early enough the contracture can be overcome by active or passive movements but if the shortening of a muscle is maintained for some weeks it cannot be immediately extended without structural damage It has also been shown that this fixation only occurs when muscle innervation is intact (*Frohlich* and *Meyer* 1920) The change is more noticeable in growing rabbits than in those of full age when tested (*Crawford* 1934) In growing rabbits muscle growth is so inhibited that shortening remains permanent and full development is never recovered even if immobilisation ceases (*Alder Crawford* and *Edwards* 1959) Some writers maintain that a contractured muscle of this kind is histologically normal (*Ranson* and *Sams* 1928 *Alder Crawford* and *Edwards* 1959) but as *Ferguson Vaughan* and *Ward* (1957) remark the literature contains highly divergent conceptions of the histological changes involved in myostatic contracture The old physiological law which states that stretched muscles (including fascia and tendons) remain insufficient and that shortened soft tissues contract is applicable to myostatic contracture

According to the present study plaster immobilisation or other fixation in a certain position such as equinovarus causes a permanent postural deformity in the growing rabbit After immobilisation of shorter duration the posture and mobility of joints returned to normal and no permanent deformity developed This makes an interesting comparison with the results obtained by *Ferguson Vaughan* and *Ward* (1957) in their study of disuse atrophy of muscle in rabbits There appeared to be no essential histological change after two weeks of immobilisation but after four weeks a lesion could be recognized In the present tests the main issue may be the myostatic contracture of soft tissues already described

Three to four weeks of immobilisation are scarcely long enough for the development of bone changes which would keep the foot in a deformed position after immobilisation is ceased The explanation of this may be found in muscle tendon ligament and/or cartilage changes In the present tests at least, radiological observation has so far *revealed no morphological* bone changes These appear later if the position of deformity is maintained

The permanent deformities achieved by the fixation method in the present study are presumably based on a similar influence they developed when a hind foot was placed in equinus and varus position by means of nylon suture Tests were performed on 5 day old rabbits and immobilisation was maintained for several weeks With several test animals *in which* the thread came loose in the course of a few weeks the deformity did not remain permanent but corrected itself within one week

It is interesting to compare the results of *Spencer* and *Pellier* (1964) when they produced plantar flexion and ulnar deviation of the fore foot *by means* of silk thread in a fetal rabbit 6—7 days before birth The thread was removed on the day of delivery Eight rabbits born with deformities lived for more than 3 days and 3 of these lived at least 6 weeks In all except one the deformity corrected itself within one week after birth One rabbit had persistent ulnar deviation and X rays of the *limb* revealed a synostosis of the radius and ulna at the point where the suture had passed through the forearm In these experiments in fact no permanent deformity provoked by a fixed position remained Apart from the fact that their rabbits were operated on a few days before birth and in present study a few days after the most noticeable difference is that immobilisation with silk suture lasted only one week in their experiments and over 3 weeks in this investigation On the basis of my results it was not expected that any permanent deformity would remain and our results are thus parallel

B TALIPES EQUINOVARUS IN MAN AND IN THE RABBIT

1 Morphological changes in bones

Many common points can be noted when the morphological and pathoanatomical bone changes of talipes equinovarus deformities produced in rabbits are compared with analyses of these deformities in man

If the experimental club foot deformities produced are examined 2—4 months after operation changes can be noted in the morphology of individual bones as well as in the positions of bones in relation to

each other These correspond significantly to the bone changes encountered in recently published reports of careful dissections of talipes equinovarus (*Bechtol* and *Mossman* 1950 *Irani* and *Sherman* 1963 *Settle* 1963 *Reimann* 1967) The principal change is in the neck of the talus which is deviated medially and plantarward on the body In addition the navicular articular surface of the talus faces medially and plantarward The calcaneus is almost normal in contour but somewhat smaller than normal in size The talonavicular and calcaneocuboidal joints are not in the frontal plane as is normal but turned medially and plantarward The talo-calcaneal angle is diminished The navicular is slightly smaller than normal and has moved medially near the medial malleolus in extreme cases Cuneiforms cuboides and metatarsals are almost normal in shape and size The posterior part of the calcaneus is often inclined towards the region of the lateral malleolus where an accessory joint is formed

2 **Soft tissue changes**

When the club foot deformities produced in rabbits are examined from the functional point of view changes can be observed similar to those encountered in man If the Achilles tendon in the rabbit is strongly tightened it can be clearly seen to exert a supinatory action and to cause a slight varus in the sole of the foot Mere attachment of the Achilles tendon in a week old rabbit causes a tendency towards the same phenomenon which disappears however during growth and with use of the foot No progressive deformity ensues and further factors are evidently needed for its development in test animals Mere extensor insufficiency apart from Achilles tension was unable to cause equinovarus deformity in the experiments Peroneal insufficiency was also required If severing of the peroneus was combined with fixation of the Achilles tendon the result was varus and slight adduction of the fore foot combined with dorsiflexion rather than equinus In accordance with this are the club foot dissections of the newborn made by *Adams* 1855 He found changes in the gastrocnemius tibialis anterior and tibialis posterior muscles All three muscle bellies were shortened In 1959 *Wiley* noted the same phenomenon in his anatomical studies where in cases of club-foot among small children muscle bellies were shorter and narrower The principal muscles affected were the gastrocnemius and soleus tibialis posterior and tibialis anterior

In examining experimental equinovarus deformities I observed the same phenomenon as *Stewart* (1951) in his anatomical study of club-foot that the Achilles tendon seems to attach itself to the medial part of the

Three to four weeks of immobilisation are scarcely long enough for the development of bone changes which would keep the foot in a deformed position after immobilisation is ceased The explanation of this may be found in muscle-tendon ligament and/or cartilage changes In the present tests at least radiological observation has so far revealed no morphological bone changes These appear later if the position of deformity is maintained

The permanent deformities achieved by the fixation method in the present study are presumably based on a similar influence they developed when a hind foot was placed in equinus and varus position by means of nylon suture Tests were performed on 5 day old rabbits and immobilisation was maintained for several weeks With several test animals in which the thread came loose in the course of a few weeks the deformity did not remain permanent but corrected itself within one week

It is interesting to compare the results of *Spencer* and *Peltier* (1964) when they produced plantar flexion and ulnar deviation of the fore-foot by means of silk thread in a fetal rabbit 6—7 days before birth The thread was removed on the day of delivery Eight rabbits born with deformities lived for more than 3 days and 3 of these lived at least 6 weeks In all except one the deformity corrected itself within one week after birth One rabbit had persistent ulnar deviation and X rays of the limb revealed a synostosis of the radius and ulna at the point where the suture had passed through the forearm In these experiments in fact no permanent deformity provoked by a fixed position remained Apart from the fact that their rabbits were operated on a few days before birth and in present study a few days after the most noticeable difference is that immobilisation with silk suture lasted only one week in their experiments and over 3 weeks in this investigation On the basis of my results it was not expected that any permanent deformity would remain and our results are thus parallel

B TALIPES EQUINOVARUS IN MAN AND IN THE RABBIT

1 Morphological changes in bones

Many common points can be noted when the morphological and pathoanatomical bone changes of talipes equinovarus deformities produced in rabbits are compared with analyses of these deformities in man

If the experimental club foot deformities produced are examined 2—4 months after operation changes can be noted in the morphology of individual bones as well as in the positions of bones in relation to

affect their physiology and ability to stretch and contract normally and may be a cause of the recurrence of club-foot deformity

In accordance with the present investigation are the interesting observations by *Flinchum* (1953) on the dissection of a six and a half month fetal club-foot The contour and relative size of individual bones in the club-foot and the normal foot appeared identical in the fetus at this stage of fetal growth But the author noted that the Achilles tendon and the tendinous part of the tibialis anterior muscle were longer in the club-foot than in the healthy foot The tibialis anterior muscle was the only structure which offered abnormal resistance to eversion. The mass of the peroneals on the affected side was only half that on the normal side He interpreted this as muscular imbalance due to dysplasia of the peroneals

Hirsch (1960) has noted under operative exposure in his series that in all patients the deltoid ligament was tight the talus anteriorly displaced and the Achilles tendon medially displaced In rabbits with equinovarus deformities very tense medial ligamentous contracture could also be found

C VERTICAL TALUS IN MAN AND IN THE RABBIT

1 Morphological and radiological changes

When experimental talus verticalis deformities were analysed and compared with clinical observations of *Langenskiold* (1964) remarkable general morphological similarities were found. In clinical examination of a talus verticalis foot in a child and in a rabbit the shape of the foot is conspicuous There is a prominence in the sole from which the heel and fore part of the foot rise in a gentle curve The general appearance is like a rocker hence the term rocker foot The head of the talus is prominent on the plantar aspect of the foot This is both visible and palpable medially Later a callus develops and sometimes also an ulceration over the prominent head of the talus When the fore part of the foot moves into dorsiflexion the distinct convexity is accentuated.

Remarkable similarities have been observed in radiological studies of the skeleton of the foot in children and rabbits with vertical talus The most important was that the distal portions of the calcaneus and talus rotate towards the plantar surface the talus rotating into a vertical position. The subtalar joint appear intact with the exceptions that the plane of the joint is more vertical and the talus is further forward on the calcaneus than in the normal foot There is an abnormal articu

calcaneus which was inclined to varus. Muscle imbalance combination leading to equinovarus in rabbit also agrees with *Stewart's* proposition: a positive deforming force + a negative deforming force. He states that the triceps surae, the tibialis anterior and minor plantar muscles exert a positive deforming force, while the peroneus muscles, deprived of their postural activity, cannot function to inhibit the distortion. Except that the combination of fixation of the Achilles tendon, tenodesis or external transection of peroneus and extensor digitorum longus led to equinovarus deformity, it could be noted on the other hand that transection of the tibialis anterior prevented its development. It appeared that the pull of the tibialis anterior was important for the medial dislocation of the navicular and also the beginning of metatarsus varus for after the discision of the tibialis anterior this transference did not occur. The deforming effect of the tibialis anterior in present tests are in accordance with the observations of *Garceau* and *Manning* (1947) on the imbalance between the invertor and evertor muscles. They recommend the transfer of tibialis anterior more laterally in the tarsus in cases of recurring club foot like many others (*Durbin* 1950, *Critchley* and *Taylor* 1952).

Without going further into the many soft tissue operations which were performed later, it may be mentioned that in 1888 *Vincent Jackson* announced a successful cure for congenital club foot immediately after severing the Achilles tendon and the tendons of the tibialis anterior and the tibialis posterior. It was probably *Lorenz* in 1784, however, who first severed the Achilles tendon in order to correct club foot. Many others have later recommended the use of a soft tissue operations directed at the release of the contractions of the Achilles tendons and the tendons of the tibialis anterior, the tibialis posterior and the flexor digitorum longus and the capsules and ligaments on the medial side of the foot (*Codivilla* 1906, *Bankart* 1922, *Brockman* 1930, *McCauley* 1959, *Pasila* and *Sulamaa* 1961). My animal experiments are in accordance with these operations.

Observations made by *Bechtol* and *Mossmann* in 1950 on muscle changes after dissection of two club foot fetuses are also consistent with present experimental results. They support the theory that faulty muscle development is an important link in the pathogenetic chain of congenital club foot. The gastrocnemius, soleus, tibialis posterior, flexor hallucis longus and flexor digitorum longus muscles showed the presence of many abnormal embryonic muscle fibres. Failure of these muscles to lengthen at the same rate as the bones of the skeleton may be the cause of the inversion of the foot. Failure in development of these muscles may

merely the ligamentum transversum cruris tightening of the extensor group was more severe than the tibialis anterior so that the final result was of the extensor type This could also be noted immediately after severing the ligament following which the sole was drawn into abduction and valgus *Herndon* and *Heyman* (1963) said that the foot as a whole is fixed in valgus and cannot be inverted But *Mead* and *Anast* (1961) wrote that the fore foot need not be in valgus as is implied sometimes in the literature The latter view agrees with present experimental results in which to be sure the extensor type was in valgus in the fore foot but the so called tibialis anterior type showed a tendency towards varus in the fore foot this is due to the elevation of the first metatarsal secondary to tightening of the tibialis anterior and transference of the point at which the pull is exerted *Franke* (1901) has also noted that in congenital flat foot in man the tendon of tibialis anterior was not inserted on the plantar aspect of the first metatarsal and the first cuneiform but on the dorsal surface

Closer analysis of experimental specimens and operative findings in children showed further similarities in dorsiflexion contracture In both of the above categories adhesions developed in the tarsus and the peroneal and extensor tendons became so fixed that their normally more distal pull had been transferred to the dorsum pedis in the tarsal region

D CONCLUSIONS

In this investigation it was possible to produce foot deformities in newborn rabbits phenotypically similar to human congenital foot deformities especially talipes equinovarus and vertical talus deformities by means of surgical and non surgical soft tissue procedures Apart from equinovarus and vertical talus deformities produced in rabbits other mutations of the foot deformities encountered in children such as talipes equinus calcaneus and varus cavus calcaneovalgus and metatarsovarus have also been similarly produced in rabbits by means of operations on soft tissues a report will be published later

An attempt was made to elucidate the peripheral mechanisms of foot deformities in experiments and to compare these with observations in humans It seemed clear that the talipes equinovarus and vertical talus changes produced in experiments were closely related to mechanical factors The same procedures could lead to the occurrence of either of the deformities The talus was in the key position in both and the manner

lation of the navicular with the upper surface of the neck of the talus In their studies *Hark* (1950) and *Hareson* (1959) have precisely described this phenomenon and its importance in the development of deformity There is also a widening of the calcaneocuboid joint and the cuboid is somewhat displaced upward at the calcaneocuboid articulation. The calcaneus is in the equinus position and the posterior part of the heel fails to touch the ground on standing The anterior portion of the calcaneus deviates in a lateral direction The calcaneus is generally underdeveloped and is convex on its plantar surface The long axis of the talus the keystone of the deformity is almost in line with the axis of the tibia This bone becomes narrow at the waist and resembles an hourglass A moulding of the navicular occurs later

2 Soft tissue changes

In vertical talus in rabbits the Achilles tendon was tight In the opinion of some authors this is not always so in vertical talus in man It has been a relative phenomenon in some cases in our clinical examinations (*Langenskiold* and *Ritsila* 1964) at least and can remain unnoticed in routine examination In the position of deformity with the fore foot in dorsal flexion and abduction the Achilles tendon is not stretched but when the position is corrected to normal the Achilles tendon is seen to tighten so that in these cases too Achilles tautness is present whether it is a primary or secondary factor

The fore foot of rabbits with vertical talus was in dorsiflexion This was maintained by the tautness of the soft tissue structures ventral to the ankle Many authors dealing with vertical talus in man have directed their attention to this dorsiflexion contracture (*Hark* 1950 *Lloyd Roberts* and *Spence* 1958) *Lamy* and *Weissman* (1939) said that the contracted extensor tendons can be felt as prominent and resisting all correction *Herndon* and *Heyman* (1963) said that the peroneal and extensor tendons may be taut and may resist passive inversion

Examinations of both rabbits and children with vertical talus reveal as shown earlier that dorsiflexion contractures may exist either in the extensor peroneus group or in the tibialis anterior muscle Thus it has been possible to distinguish these so called extensor and tibialis anterior types Both types have also been encountered later in children at operation (*Langenskiold* 1964) In tests where neither the extensor digitorum longus muscle nor the tibialis anterior muscle was severed but change in their action and myostatic contracture were produced by severing

merely the ligamentum transversum cruris tightening of the extensor group was more severe than the tibialis anterior so that the final result was of the extensor type This could also be noted immediately after severing the ligament following which the sole was drawn into abduction and valgus *Herndon* and *Heyman* (1963) said that the foot as a whole is fixed in valgus and cannot be inverted But *Mead* and *Anast* (1961) wrote that the fore foot need not be in valgus as is implied sometimes in the literature The latter view agrees with present experimental results in which to be sure the extensor type was in valgus in the fore foot but the so called tibialis anterior type showed a tendency towards varus in the fore foot this is due to the elevation of the first metatarsal secondary to tightening of the tibialis anterior and transference of the point at which the pull is exerted *Franke* (1901) has also noted that in congenital flat foot in man the tendon of tibialis anterior was not inserted on the plantar aspect of the first metatarsal and the first cuneiform but on the dorsal surface

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in which the fore foot changed position especially in the talonavicular joint was decisive In talus verticalis the fore foot moved into dorsiflexion abduction and eversion In talipes equinovarus it moved into plantar flexion or equinus adduction and inversion *Osmond Clarke* (1956) suggested that club foot is essentially a talonavicular and subtalar subluxation and vertical talus is a subluxation at the same joints but with displacement in the opposite direction It is interesting that *Herndon* and *Heyman* (1963) too were inclined to believe that congenital convex pes valgus or vertical talus is closely akin to a club foot in etiology

The present author has assumed that a peripheral primary fault in different congenital foot deformities which may differ in their etiology is of a similar nature This peripheral fault may lie in the muscles or other soft tissues The resultant bony deformity was thus assumed to be extrinsic not intrinsic secondary not primary The results confirm these assumptions

Soft tissue contractures and combinations of them resembling those encountered in man have been produced in rabbits It has also been verified that they cause corresponding structural deformities of the bones Thus soft tissue changes have exerted a controlling influence on bone growth evidently following of bone transformation suggested earlier (*Hueter* 1862 *v Volkmann* 1869 *Wolff* 1892)

VI SUMMARY

The aim of this study was to produce in young rabbits imitations of the congenital foot deformities encountered in man by provoking changes in the soft tissues

A total of 76 separate procedures were performed Approximately 500 rabbits were used 402 for actual tabulated procedures and the rest for preliminary tests

By means of transections and resections of tendons and muscles tenodeses transections of ligaments and fixation in plaster in extreme positions it was found possible to produce a number of imitations of foot deformities found in humans those corresponding to talipes equinovarus and vertical talus are described The age of the rabbits at operation varied from 4 to 28 days most of them being from 6 to 7 days old

Marked talipes equinovarus deformity was produced in 32 rabbits and vertical talus in 51 The course of development of the deformity was followed during growth by repeated radiography The deformities produced were analyzed by dissection and photography of the feet of 75 animals killed at different ages Sections for histological examination were taken from 8 animals

In both a macro-and micro anatomical and a radiological sense great similarities were observed between the deformities in rabbits and those encountered in humans

Talipes equinovarus was produced by operation on the soft tissues by using only a combination of Achilles tenodesis transection of the extensor digitorum longus muscle and transection of both peroneal muscles Sufficiently long immobilisation in the equinovarus position 3—4 weeks also led to a permanent even progressive equinovarus deformity A resemblance in general structure between such deformities in rabbits and humans was noted (Fig 4 p 34) including the interrelation of bones of the feet (Figs 5 6 7 8 pp 36 37) the radiological examination (Figs 9 10 pp 38 39) the changes in the shape of individual bones (Figs 11 12 pp 41 42) the changes in soft tissues (Fig 13 p 45) and the microscopic examination (Fig 14 p 47)

Vertical talus deformity was produced most easily by causing simultaneous contracture of the triceps surae muscle group and the dorsiflexor muscles of the foot Myostatic contracture was caused by plaster or other immobilisation and transection of the ligamentum transversum cruris or Achilles tenodesis was used instead of the triceps surae contracture provoked by immobilisation in the equinus position By combining these measures with transections of either the tibialis anterior or the extensor digitorum longus on the dorsiflexor side of the foot two separate types of vertical talus deformity were produced These two types have also been discerned in a series of vertical talus feet in children (*Langenskiold* 1964) Similarities have also been noted in the general structure of experimental vertical talus deformities in rabbits and human vertical talus deformities (Figs 17 18, 19 20 pp 54 55) and in the interrelation of bones (Figs 21 22 23 pp 57 58 59) In the same way radiological comparison (Figs 24 25 26, pp 61 62 63) and comparison of the shape of the talus (Figs 27 28 pp 65 66) in relation to descriptions given in the literature show distinct similarities Muscular and ligamentous contracture of the vertical talus in rabbits and in humans was found to be very similar (Fig 29 p 69) A resemblance was also noted in the microscopic comparison (Fig 30 p 70)

The results of the present study confirm the importance of considering primary soft tissues changes as a factor provoking secondary skeletal deformities

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APPENDIX

Seven series of pictures describing development and progression of the talipes equinovarus and vertical talus deformities produced by various procedures in newborn rabbits

In each picture from left to right normal foot in lateral projection deformed foot in lateral projection normal foot in dorsoplantar projection and deformed foot in dorsoplantar (or antero-posterior) projection

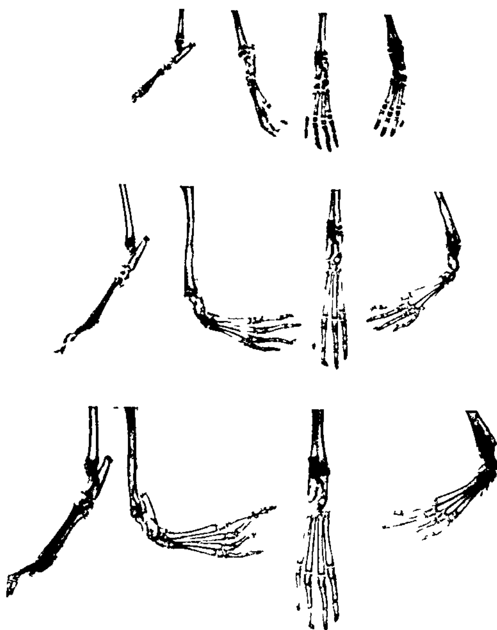


FIG. 31. Development and progression of the talipes equinovarus deformity in a rabbit. Series XXVI, no. 10.

Top: lateral and dorsoplantar roentgenograms one week after Achilles tenodesis, transection of the extensor digitorum longus and peroneal muscles, and transection of the ligamentum transversum cruris.

Centre: six weeks. Bottom: six months after operation.

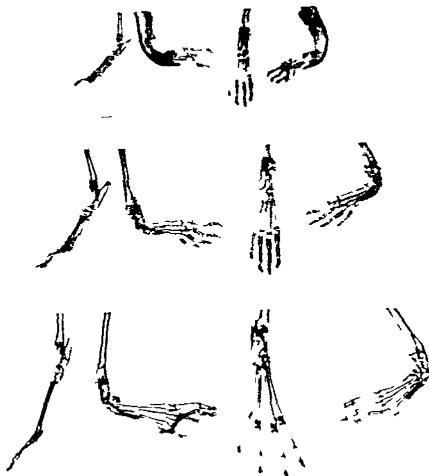


Fig. 3. Development and progression of the talipes equinovarus deformity in a rabbit produced by plaster immobilisation in equinovarus position. Series LIX no. 1.

Top: lateral and dorsoplantar roentgenogram one week after immobilisation. Centre: six weeks; bottom: six months after immobilisation, immobilisation removed.

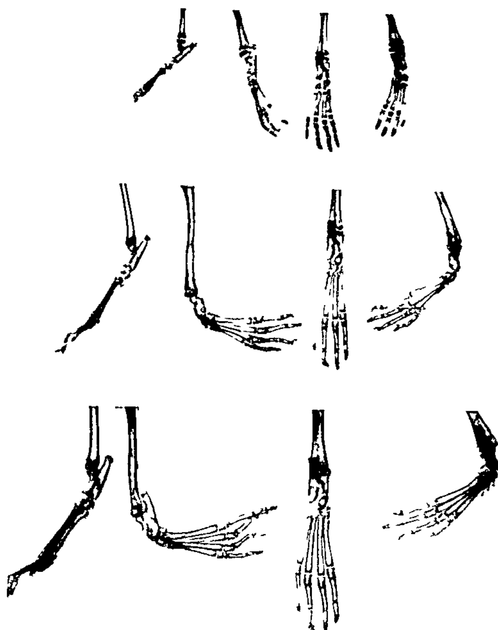


FIG. 31. Development and progression of the talipes equinovarus deformity in a rabbit. Series XXVI no. 10.

Top: lateral and dorsoplantar roentgenograms one week after Achilles tenodesis, transections of the extensor digitorum longus and peroneal muscles, and transection of the ligamentum transversum cruris.

Centre: six weeks. *Bottom:* six months after operation.

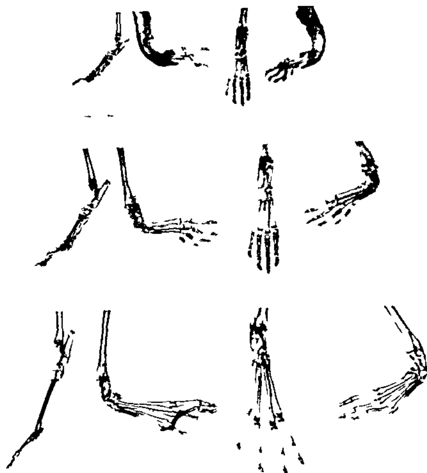


FIG 32 Development and progression of the talipes equinovarus deformity in a rabbit produced by plaster immobilisation in equinovarus position Series I IX no 1

Top lateral and dorsoplantar roentgenograms one week after immobilisation

Centre six week bottom six months after immobilisation immobilisation removed

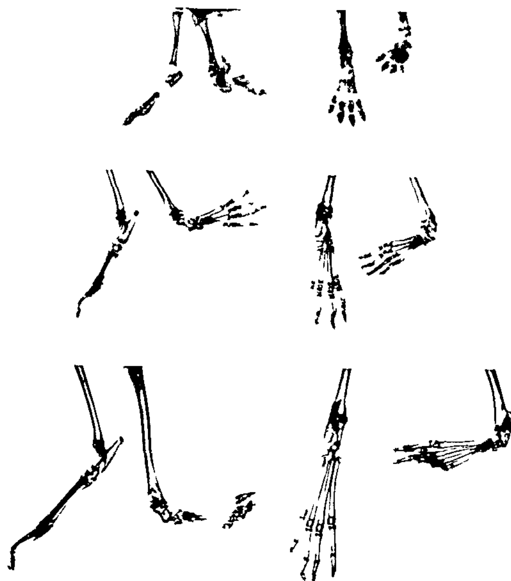


FIG 33 Development and progression of the talipes equinovarus deformity in a rabbit produced by fixation with nylon thread in equinovarus position Series XII no 7

Top lateral and dorsoplantar roentgenograms one week after fixation
Centre six weeks bottom six months after fixation fixation removed



FIG 34 Development and progression of the vertical talus deformity in a rabbit The extensor digitorum type Series XII no 2

Top lateral and dorsoplantar (or anteroposterior) roentgenograms one week after Achilles tenodesis transections of the tibialis anterior muscle and the ligamentum transversum cruris

Centre six weeks bottom six months after operation

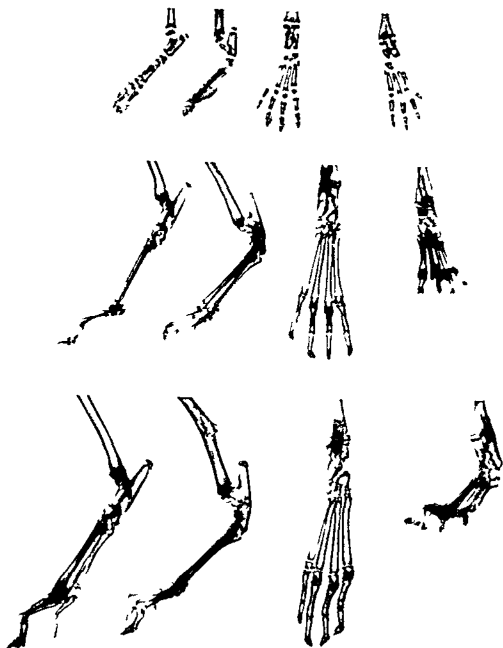


FIG. 35. Development and progression of the vertical talus deformity in a rabbit. The tibialis anterior type. Series *II* no.

Top: lateral and dorsoplantar (or anteroposterior) roentgenograms one week after Achilles tenodesis, transections of the extensor digitorum longus and peroneal muscles, and transection of the ligamentum transversum cruris.

Centre: six weeks. Bottom: six months after operation.

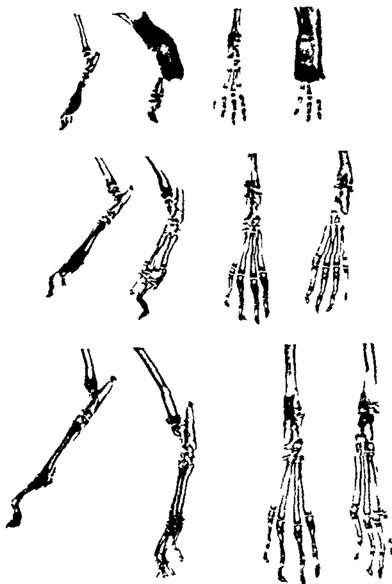


FIG 3(Development and progression of the vertical talus deformity in a rabbit produced by plaster immobilisation in equinus position and transection of the ligamentum transversum cruris Series I XI no 3

Top lateral and dorsoplantar roentgenograms one week after operation

Centre six weeks bottom six months after operation

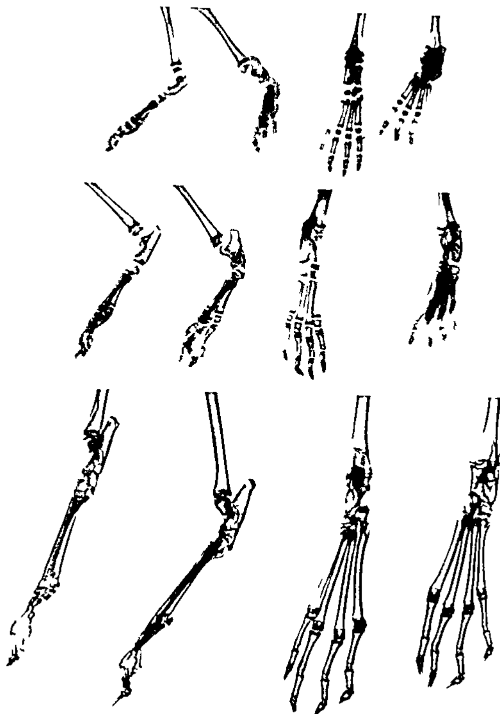


FIG 37 Development and progression of the vertical talus deformity in a rabbit produced by fixation with nylon thread in equinus position Series XII no 6
Top lateral and dorsoplantar roentgenograms one week after fixation
Centre six weeks bottom six months after fixation fixation removed

ERRATA

Page 29 Table 2 right side line No 4 from below for $A_T + TA_T + P_T$ read $A_T + TA_F + P_T$

Page 30 Table 2 right side Fixation in calcaneovarus position strike out the number 1 in column Number of vertical talus Fixation in equinus position insert the number 1 in column Number of vertical talus

Page 31 Table 3 line No 8 from above for $A_T + TA_T + P_T$ read $A_F + TA_T + P_T$

Page 33 Line No 6 from above for discisions read discissions

Page 33 Lines No 2 and No 14 from below for tibialis posterior read tibialis posterior

Page 44 Line No 26 from above for posterior read posterior

Page 50 Table 4 line No 4 from above for mucle read muscle

Page 50 Table 4 line No 21 from above for No 2 read No 4

Page 50 Table 4 line No 5 from below for in calcaneovarus read in equinus

Page 64 Line No 3 from below for phenomen read phenomenon

Page 67 Lines No 3 and No 17 from below for dorsiflexion read dorsiflexor

Page 79 Line No 12 from below for non surgigical read non surgical

Page 82 Line No 2 from below for tissues read tissue

Page 96 Line No 2 from above for Series I I no 2 read Series XXVII no 1

Page 98 Line No 2 from above for Series XII no 6 read Series XII no 3

SVEN ERIK LARSSON

ON THE DEVELOPMENT OF OSTEOPOROSIS

EXPERIMENTAL STUDIES IN THE ADULT RAT

CONTENTS

ACTA ORTHOPAEDICA SCANDINAVICA
SUPPLEMENTUM No 120

From the Department of Orthopaedic Surgery (Head Prof J Sevastikoglou M D)
University Hospital Umeå Sweden

ON THE DEVELOPMENT OF OSTEOPOROSIS

EXPERIMENTAL STUDIES IN THE ADULT RAT

BY
SVEN ERIK LARSSON

The paper on bone glycosaminoglycans written together with Dr Lars Vejlens Institute of Pathology (Head Prof B Engfeldt, M D) University of Uppsala Uppsala Sweden

CONTENTS

CENTRALTRYCKERIET UMEÅ 1969

CONTENTS

PREFACE

My sincere thanks are due to all those whose help in a variety of ways has been a prerequisite for realization of this investigation.

To Professor John Sevastikoglou, Head of the Department of Orthopaedic Surgery, University Hospital, Umeå, my *chief and teacher*, who originally suggested the subject of this study, *for his personal interest* and for generous aid in planning and carrying through the investigation.

To Professor Tor Hiertonn, Head of the *Department of Orthopaedic Surgery*, University Hospital, Uppsala, for the years spent in the stimulating athmosphere of his clinic.

To Professor Bengt Engfeldt, Head of *the Institute of Pathology*, University of Uppsala, for the privilege of using his laboratory *facilities for the work* on bone glycosaminoglycans.

To Docent Sven Olof Hjertquist for generous help in methodological *questions* in the work on bone glycosaminoglycans.

To Docent Rudolf Lemperg for helpful criticism and advice.

To Laborator Karl Johan Öbrink and Docent Göran Östling, Institute of Physiology, University of Uppsala, for technical aid in Ca^{45} activity determinations.

To Lennart Gustafsson, F.K., for valuable help with the statistics.

To Miss Maud Marsden for correction of the use of the English language.

The work was supported by grants from the Swedish Medical Research Council, King Gustaf the Fifth's Eightieth Birthday Fund, The Faculty of Medicine, University of Uppsala and the Faculty of Medicine, University of Umeå, Sweden.

INTRODUCTION

DEFINITION

The definition of osteoporosis is the least controversial aspect of an otherwise highly controversial subject (*Rose* 1967) According to the generally accepted definition osteoporosis is a condition resulting from a widespread lack of bone with no detectable chemical abnormality in the bone that remains (*Albright and Reifenstein* 1948 *Nordin* 1961 *Lafferty et al* 1964 *Dent and Watson* 1966 *Rose* 1967) Although this definition has never been seriously challenged there are reports according to which it would not hold true Thus osteoporotic bone has been found to show cellular differences from the normal *i e* an increased frequency of devitalized osteocytes and empty lacunae (*Urist et al* 1963) and disturbed bone cell metabolism as measured *in vitro* (*Nichols Jr and Flanagan* 1966) A slight but definite reduction in the calcium content and the Ca P ratio of osteoporotic bone has been reported by *Birkenhaeger Frenkel et al* (1961) Results of studies on the composition of microscopic bone structures from human material of varying ages indicate changes in the contents of calcium phosphorus and nitrogen measured as percentage by weight (*Strandh and Norlen* 1965) Changes in organic bone matrix have been reported from studies with the aid of X ray diffraction and electron microscopy (*Little et al* 1962) In osteoporotic subjects decreased hydroxyproline contents have been found in bone specimens from the iliac crest (*Birkenhaeger Frenkel* 1966) Biochemical studies (*Cassucio et al* 1962) indicate a decrease with age in protein nitrogen and polysaccharides and changes in the glucosamine/galactosamine ratio in fractions of vertebral bone tissue extracted according to *Dische et al* (1958) The qualitative changes in bone matrix observed by *Little et al* (1962) and *Cassucio et al* (1962) have been related to the osteoporotic process The significance of this as a pathophysiological mechanism remains to be determined however

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In hypogonadism osteoporosis may occur both in males and females (*Albright et al* 1942) and the hypothesis that oestrogen deficiency is the cause of human osteoporosis was advanced by *Albright and Reifenstein* (1948) This hypothesis was extended later to include the possibility that senile and other forms of osteoporosis are caused by an imbalance between anabolic or gonadal hormones and anti anabolic or adrenal corticoid hormones (*Reifenstein* 1957 *Urist and Vincent* 1960) The role of the menopause in the occurrence of osteoporosis has been emphasized by radiological observations of a fall in bone density corresponding in time to the menopause (*Jasani et al* 1965 *Meema et al* 1965 *Meema* 1966 *Nordin et al* 1966) However only a low degree of correlation between age at the menopause and age at the onset of symptomatic osteoporosis was found by *Saville* (1967) in a study of women who had had a surgical and women with a natural menopause The menopause would then be only one of different factors of importance for the occurrence of osteoporosis The original concept of *Albright et al* (1940) that involutional osteoporosis is due to osteoblastic failure consequent to a deficiency of gonadal hormones has been made untenable by results of more recent investigations with refined morphological techniques and of calcium balance and radiocalcium kinetic studies It has been concluded from results of these studies that new bone formation is commonly normal in postmenopausal and senile osteoporosis (*Heaney and Whedon* 1958 *Nordin* 1960) and that osteoblastic activity does not diminish with age (*Jowsey* 1960 *Frost and Villanueva* 1961) Instead bone resorption appears to be markedly increased in osteoporosis (*Frost* 1961 *Riggs et al* 1964)

Hypercorticoidism of endogenous origin is often associated with osteoporosis (*Albright and Reifenstein* 1948 *Follis* 1951 *Iannaccone et al* 1960 *Storey* 1963) In prolonged cortisone therapy osteoporosis is a serious complication (*Burns et al* 1955 *Reifenstein* 1958 *Rosenberg* 1958) however there are reports suggesting that the contribution of other factors may be necessary for the development of corticosteroid osteoporosis Thus 85 per cent of the patients of comparable ages and skeletal conditions do not develop osteoporosis on comparable steroid therapy (*Schlesinger et al* 1961) It has not been possible to relate the incidence of fractures to the dose of steroids or to the duration of treatment (*McConkey et al* 1962) In patients with allergic diseases treated with steroids only a small effect on the skeleton has been reported (*Krokowski and Stresemann* 1967)

Of the nutritional disturbances scurvy leads to radiological signs of osteoporosis in adults and has recently been studied in Johannesburg Bantu (*Seftel et al* 1966) However the clinical picture in these subjects is confused by the presence of hepatic siderosis and other factors (*Dent and Watson* 1966)

CLINICAL OSTEOPOROSIS

Osteoporosis is not a single disease entity but is a condition produced by many different factors (*Frost* 1963) Despite the varying aetiology the end result — osteoporosis — is now a well recognized condition and justifies its description by a single term (*Dent and Watson* 1966) In the following table the main causes have been listed according to *Rose* (1967)

THE MAIN CAUSES OF OSTEOPOROSIS

1 *Endocrine disturbances*
  - Hypogonadism
  - Cushing s syndrome
  - Cortisone administration
  - Acromegaly
  - Thyrotoxicosis

2 Nutritional disturbances
  - Scurvy
  - Calcium deficiency
  - Protein deficiency

3 Idiopathic
  - Juvenile
  - Pregnancy
  - Postmenopausal
  - Senile

4 Inherited
  - Osteogenesis imperfecta

5 Immobilization

In the numerous attempts made in the past to find the aetiological agents which could provide the clues to the pathogenesis of idiopathic osteoporosis endocrine and nutritional disturbances have been extensively studied in this respect

Of the endocrine disturbances thyrotoxicosis is considered by some authors to give rise to osteitis fibrosa rather than osteoporosis (*Follis* 1953 *Rose* 1967) In acromegaly the predominant bone disorder does not seem to be osteoporosis but a chang distribution of spongious and compact bone in the keleton (*Jesserer* 19)

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5 Immobilization

In the numerous attempts made in the past to find the aetiological agents which could provide the clues to the pathogenesis of idiopathic osteoporosis endocrine and nutritional disturbances have been extensively studied in this respect

Of the endocrine disturbances thyrotoxicosis is considered by some authors to give rise to osteitis fibrosa rather than osteoporosis (*Follis* 1953 *Rose* 1967) In acromegaly the predominant bone disorder does not seem to be osteoporosis but a change distribution of spongious and compact bone in the skeleton (*Jesserer* 196

In hypogonadism osteoporosis may occur both in males and females (*Albright et al* 1942) and the hypothesis that oestrogen deficiency is the cause of human osteoporosis was advanced by *Albright and Reifenstein* (1948) This hypothesis was extended later to include the possibility that senile and other forms of osteoporosis are caused by an imbalance between anabolic or gonadal hormones and anti anabolic or adrenal corticoid hormones (*Reifenstein* 1957 *Urist and Vincent* 1960) The role of the menopause in the occurrence of osteoporosis has been emphasized by radiological observations of a fall in bone density corresponding in time to the menopause (*Jasani et al* 1965 *Meema et al* 1965 *Meema* 1966 *Nordin et al* 1966) However only a low degree of correlation between age at the menopause and age at the onset of symptomatic osteoporosis was found by *Saville* (1967) in a study of women who had had a surgical and women with a natural menopause The menopause would then be only one of different factors of importance for the occurrence of osteoporosis The original concept of *Albright et al* (1940) that involutional osteoporosis is due to osteoblastic failure consequent to a deficiency of gonadal hormones has been made untenable by results of more recent investigations with refined morphological techniques and of calcium balance and radiocalcium kinetic studies It has been concluded from results of these studies that new bone formation is commonly normal in postmenopausal and senile osteoporosis (*Heaney and Whedon* 1958 *Nordin* 1960) and that osteoblastic activity does not diminish with age (*Jowsey* 1960 *Frost and Villanueva* 1961) Instead bone resorption appears to be markedly increased in osteoporosis (*Frost* 1961 *Riggs et al* 1964)

Hypercorticoidism of endogenous origin is often associated with osteoporosis (*Albright and Reifenstein* 1948 *Follis* 1951 *Iannaccone et al* 1960 *Storey* 1963) In prolonged cortisone therapy osteoporosis is a serious complication (*Bunim et al* 1955 *Reifenstein* 1958 *Rosenberg* 1958) however there are reports suggesting that the contribution of other factors may be necessary for the development of corticosteroid osteoporosis Thus 85 per cent of the patients of comparable ages and skeletal conditions do not develop osteoporosis on comparable steroid therapy (*Schlesinger et al* 1961) It has not been possible to relate the incidence of fractures to the dose of steroids or to the duration of treatment (*McConkey et al* 1962) In patients with allergic diseases treated with steroids only a small effect on the skeleton has been reported (*Krokowski and Stresemann* 1967)

Of the nutritional disturbances scurvy leads to radiological signs of osteoporosis in adults and has recently been studied in Johannesburg Bantu (*Seftel et al* 1966) However the clinical picture in these subjects is confused by the presence of hepatic siderosis and other factors (*Dent and Watson* 1966)

Protein deficiency has been alleged to cause osteoporosis in humans However in the majority of subjects the bone lesion appears to be both osteoporosis and osteomalacia due to lack of vitamins as well as other deficiences (*Jesserer* 1963)

The role of pure calcium deficiency in the pathogenesis of osteoporosis is controversial *Albright and Reifenstein* (1948) and *Rose* (1967) among others have considered that specific calcium deficiency is not of primary aetiological importance while other authors (*Whedon* 1959, *Nordin* 1960 *Fraser* 1962) have emphasized the possible role of dietary calcium in the pathogenesis Although some dietary surveys have shown a normal calcium consumption in osteoporotic persons (*Urist* 1960 *Smith and Frame* 1965) and little relation between mild osteoporosis and calcium intake (*Nordin* 1964) other studies have shown a lower mean calcium intake in osteoporotic than in normal persons (*Nordin* 1961 *Lutwak* 1964) and that severe osteoporosis only seems to occur in individuals on a low calcium intake (*Nordin* 1964) However man has a considerable ability to adapt to restricted calcium intake by enhanced intestinal absorption or by decreased urinary excretion (*Malm* 1958) and therefore any further loss of bone mineral might be prevented unless a failure of adaptation to the low calcium level occurs Some persons are however unable to adapt to calcium restriction and in these subjects a protracted negative calcium balance results (*Malm* 1958) The nature of this adaptation mechanism is unknown It seems however that osteoporotic patients are less able than normal subjects to reduce their urinary calcium (*Bhandarkar and Nordin* 1962) and calcium excretion appears to be independent of the intake in osteoporosis (*Nordin* 1961) The observed calcium requirement appears to be increased in osteoporosis (*Nordin* 1962)

During the adult life span there is a gradual decrease in bone mass which occurs more or less physiologically in all normal people Thus there is a steady loss of apparent density of whole bones from 20 years on in both sexes and in both white and negro races (*Trotter et al* 1960) These observations were confirmed by *Lindahl and Lindgren* (1962) who found a parallel decrease in bone density in the upper end of the tibia and the vertebral column with increasing age The radiographic density of bone removed at autopsy has also been reported to decrease steadily after the age of 20 years in both sexes (*Caldwell* 1962) In agreement with these findings are those of *Arnold* (1964) who showed a steady decrease from the age of 30 years in the weight of ash per unit volume of bone removed at autopsy from the lumbar vertebral cortex From 20 years on there is in both sexes a progressive increase in resorption spaces in the cortical bone (*Atkinson* 1965) These observations might indicate

a physiological progressive loss of bone in all normal people with increasing age probably due to increased bone resorption Of importance for this process is certainly the more sedatory life of old people than at younger ages Osteoporosis due to immobilization is well known It is not considered however that a more sedatory life is the prime aetiological factor in the pathogenesis rather it might be secondary to symptomatic osteoporosis and induce an additional loss of bone mineral

From the above findings *Rose (1967) drew the conclusion* that osteoporosis is a condition towards which all people progress gradually beginning soon after the age of 20 years However according to *Dent and Watson* (1966) symptomatic osteoporosis is caused by the action of an additional process which accelerates this gradual loss of bone resulting in greatly increased negative calcium balances of the order of 200—400 mg per day until the process limits itself spontaneously This additional process which is of uncertain origin thus causes acute attacks of osteoporosis and these can be observed in the young the adult and also the senile patient (*Dent* 1968) *Urist* (1959) attributed osteoporosis to the absence of a purported anti osteoporosis factor The loss of bone mass in normal aging is obviously much slower than in osteoporosis (*Urist* 1959)

In an attempt to incorporate the numerous both unrelated and contradictory observations in osteoporotic patients into a unified concept of osteoporosis *Heaney* (1965) related the osteoporotic process to calcium metabolism and to the demands placed upon the homeostasis of the extracellular fluid calcium According to this concept dietary calcium deficiency and the intestinal malabsorption syndromes may produce osteoporosis simply by presenting the organism with less mineral than is needed for minimal losses osteoporosis results because of homeostatic efficiency Relative or absolute deficiency of gonadal hormones would lead to a negative calcium balance because of increased bone resorption not so much because these hormones decrease resorption *per se* but because they appear to moderate the resorptive response of osteoclasts to homeostatic stimuli and in their absence bone becomes hyperresponsive to parathyroid hormone (*Heaney* 1965)

ANIMAL EXPERIMENTS

Calcium deficiency

There are several reports indicating that osteoporosis can be induced in animals by dietary calcium deficiency Attempts to produce rickets in animals by feeding

low calcium diets were made in the middle of the last century In 1885 *Pommer* described for the first time the characteristic features of rickets In a review article he concluded that low calcium diets caused osteoporosis not rickets (*Pommer* 1925) In a later review of the subject in 1948 *Follis noted that* rickets had been produced by low calcium *diets but that no descriptions were* available *for animals fed* diets containing optimal amounts of vitamin D More recently *Nordin* (1960) in a review, intended to show that osteoporosis could be produced in animals by a negative calcium balance, usually induced by low calcium diets However only young growing animals were studied in these experiments There were only two reports of the histological appearance of the bones resulting from a diet deficient solely in calcium where adequate amounts of vitamin D were provided (*Crawford et al* 1957 *Harrison and Fraser* 1960)

While young rats maintained on low calcium diets with adequate amounts of vitamin D have been reported to develop osteoporosis (*Crawford et al* 1957, *Harrison and Fraser* 1960) there are also reports that young growing rats fed a similar diet develop skeletal changes typical of rickets (*Park et al* 1922 *Hess* 1929 *Carttar et al* 1950 *Engfeldt et al* 1962 *Gershon Cohen et al* 1962 *McClendon and Blaustein* 1965) The experiments of *Gershon Cohen et al* (1962) suggest that low calcium diets produce rachitic lesions in the young growing rat but that when the animals attain an adult age the condition is *transformed* into osteoporosis Weaned rats maintained on low calcium diets for a *certain* period of time show signs of rickets but this changes later *into osteoporosis* without an alteration of diet (*McClendon and Blaustein* 1965) *It is therefore* considered erroneous to relate the bone lesions induced in young growing rats to osteoporosis as has been done earlier by *Crawford et al* (1957) *Harrison and Fraser* (1960) and *Fraser* (1962) Moreover calcium deficiency in young animals interferes with skeletal growth because a normal calcium intake is necessary for the growth of all tissues including bone regardless of whether other conditions necessary for calcification are present or not (*Carttar et al* 1950 *Foothill and Hosking* 1968)

The adult rat is considered to be resistent to the development of *osteoporosis* by restricted calcium intake because of its effective adaptation to a low calcium level reported in calcium balance studies (*Nicolaysen et al* 1953) There are however no earlier reports confined to studies on the effect of prolonged calcium deficiency on the skeleton of the adult rat or the pathomechanisms responsible for the skeletal changes induced by such treatment

Studies with bone seeking isotopes are inconclusive with regard to the skeletal reaction of experimental animals to prolonged calcium restriction Thus a greater retention than normal of a dose of strontium was reported by *Harrison and Fraser* (1960) while *Copp and Sucker* (1962) found a reduced retention of Ca^{45} in young rats after dietary calcium restriction In calcium deficient adult rats the data obtained indicated normal Ca^{45} retention and increased bone resorption as compared with normal controls (*Copp and Sucker* 1962) In this study the bone tissue was not studied further however

In adult cats fed a low calcium meat diet *i e* calcium 0 007 and phosphorus 0 18 per cent on a wet weight basis radiological evidence of osteoporosis was found after 10 weeks (*Jowsey and Gershon Cohen* 1964) The bone changes induced were described as osteoporosis However the appearance of resorption cavities in the cortical bone and the observed increase in number of newly formed osteones together with the described parathyroid hyperplasia suggest that the observed bone lesion could have been osteomalacia or osteitis fibrosa rather than osteoporosis This is supported by the fact that young growing dogs receiving a low calcium diet with vitamin D supplements develop erosion and resorption of bone with increase in the amount of fibrous tissue associated with the bones (*Campbell and Douglas* 1965) Similar observations have also been reported in mature dogs maintained on a low calcium high phosphorus diet In this study the condition was called nutritional hyperparathyroidism (*Saville and Krook* 1968) In a recent study on adult cats fed the low calcium high phosphorus meat diet described above an evident but transient osteomalacia was reported at 5 months on the low calcium diet while after 13 months the condition had changed into osteoporosis Also in these animals secondary hyperparathyroidism occurred (*Jowsey and Raisz* 1968) These reports indicate that the reaction of the skeleton to prolonged calcium restriction is still poorly understood and that a possible relationship between calcium deficiency and development of osteoporosis in adult mammals needs further investigation

Treatment with corticosteroids

Animal experiments have also been used for the study of osteoporosis induced by hormonal disturbances Thus osteoporosis has been reported in young rabbits after cortisone treatment (*Sissons and Hadfield* 1955 *Storey* 1957 and 1960) The similarity of these lesions to those observed in Cushing s disease was pointed out by *Sissons* (1956) From histological observations it was deduced that the

effect of cortisone is inhibitory to new bone formation and that the bone rarefaction is due to unopposed continuance of the normal osteolytic processes (*Sissons and Hadfield* 1955, *Sissons* 1956) More recently it has been concluded from morphological studies that the cortisone osteoporosis in rabbits occurs not only from a cessation of bone formation but primarily from a direct degrading effect which causes a massive resorption of bone (*deValderrama and Munuera* 1966)

The results reported from studies on the effect of cortisone on the skeleton of young growing rats are not conclusive Observed dense metaphyseal bone was believed to be due to delayed bone resorption (*Follis* 1951) Later it was reported that osteoporosis occurred only when the cortisone treated young rats were fed a diet containing a normal or lowered amount of calcium and phosphorus (*Storey* 1960) Osteoporosis has also been reported in growing male rats after prolong d cortisone therapy (*Kahn and Skoryna* 1959)

In growing male rats osteoporosis has been claimed to result from a combinat on of bilateral adrenalectomy orchidectomy and cortisone administration (*Caldwell* 1962) Administration of oestradiol cured the osteoporotic changes in these animals despite continued treatment with cortisone while administration of testosterone resulted in only very slight improvement These results suggest that this radiographically observed osteoporosis might have been caused by an excess of corticosteroids in the absence of oestradiol However since young animals were used the interference of the treatment with normal skeletal growth and development makes it difficult to interpret the results obtained

In adult cortisone treated rats the collagen content of the whole femur has been reported to be unchanged while the hexosamine content was decreased This led to the sugge tion that a decrease of mucopolysaccharides precedes the events which give rise to osteoporosis in Cushing s disease (*Sobel and Marmorston* 1954) Although changes in the hexosamine content of the whole femur must reasonably be considered as non representative of the mucopolysaccharides of the bone tissue itself this observation provides considerable interest but needs further investigation

The well known effect of corticosteroids upon the calcium metabolism must further be taken into consideration in studies concerning the pathogenesis of cortisone osteoporosis (*Heaney* 1965) The skeletal retention of bone seeking isotopes in young growing rats has been reported to be inhibited by the administration of corticosteroids (*Clark et al* 1959 *Milhaud et al* 1960 *Bohr and Dawids* 1964) Calcium excretion has consistently been found to be increased The results reported concerning the effect on intestinal calcium absorption are

not quite conclusive however The administration of hydrocortisone to young rats has been considered to inhibit the uptake by bone of Ca^{45} which was also found to be decreased in nephrectomized rats this led to the suggestion that the limiting factor may lie in the synthesis of chondroitin sulphate (*Clark et al* 1959) No reports have been found regarding the effect of combined oophorectomy and prednisolone administration on mature bone tissue

In the majority of the experimental studies reviewed young growing animals have been used and an interference between the well known growth inhibitory effect of corticosteroids and the skeletal reaction to the treatment cannot therefore be eliminated The effect of such treatment upon the adult skeleton in which calcification and growth are completed awaits further investigation especially with regard to the development of osteoporosis

SUMMARIZING REMARKS

1 Although osteoporosis is a condition with a clear and generally accepted definition there are reports indicating that this definition can no longer be considered adequate Thus cellular differences between osteoporotic and normal bone have been observed by morphological and *in vitro* metabolic studies Changes in the bone minerals have been reported from macro- and microchemical studies Finally changes in organic bone matrix have been found by physical and biochemical methods

2 In the numerous attempts made to elucidate the aetiological factors connected with the pathogenesis of osteoporosis nutritional and hormonal disturbances have been studied and considered to cause the condition The opinions expressed in this respect are controversial

3 During the normal aging of the adult skeleton there is a slow, steady loss of bone probably due to a slight increase in bone resorption

4 The opinion has been held that this steady loss of bone during normal aging *is the prime* aetiological factor for the pathogenesis of osteoporosis

5 Another opinion is that clinical osteoporosis is caused by certain aetiological factors responsible for an acceleration of the normal rate of bone loss for a limited period of time

6 Although these additional agents are still unknown nutritional and hormonal disturbances must be taken into consideration The effects on the adult skeleton of prolonged calcium restriction and an imbalance between gonadal and adrenal corticoid hormones need further investigation

7 In the pathogenesis of osteoporosis the concept of deficient new bone formation and osteoblastic failure has been abandoned Instead increased bone resorption is considered to be the predominant feature in most of the osteoporoses

8 In a unified concept of osteoporosis disturbed calcium homeostasis is considered to be the main pathophysiological mechanism responsible for induction of different osteoporoses This theory needs further proof however

9 In numerous experiments different bone lesions have been reported by maintaining animals on low calcium diets for certain periods of time The reaction of the adult skeleton to prolonged calcium restriction is however still poorly understood

10 In rabbits osteoporosis can be produced by cortisone treatment In growing rats it occurs only with normal or low intakes of calcium and phosphorus during cortisone treatment In growing animals the inhibitory effect of corticosteroids on growth interferes with the skeletal reaction to the treatment This interference must be taken into consideration especially when its relation to the development of osteoporosis is concerned

11 In adult rats there are no reports of osteoporosis produced by corticosteroids While no effect has been found on the hydroxyproline content of the whole bone the suggested decrease in the concentration of mucopolysaccarides has been related to the development of osteoporosis This needs to be investigated further

12 In growing male rats roentgenological osteoporosis develops after combined bilateral adrenalectomy orchidectomy and cortisone administration Contrary to the experience in clinical osteoporosis the skeletal lesions induced by this treatment could be cured by oestradiol Further studies regarding the reaction of the adult skeletal tissue to hormonal imbalance *e g* excess corticosteroids and lack of gonadal hormones would seem justified therefore

13 Studies on the effect of these nutritional and hormonal disturbances upon calcium homeostasis in the adult animal app ar to be of interest in the pathogenesis of osteoporosis

THE PRESENT INVESTIGATION

Concerning the pathogenesis of human osteoporosis prolonged dietary calcium deficiency and imbalance between gonadal and adrenal corticoid hormones have received the greatest interest The lack of coherent information on the effect of these disturbances upon the adult skeletal tissue with regard to the development of the condition motivated the present investigation Most previous experimental studies have been performed on young animals whereas osteoporosis is characteristically a disorder of old age While in clinical osteoporosis most of our present knowledge concerns the different features of the osteoporotic skeleton and not the development of the condition in interpreting most earlier studies of experimental osteoporosis the interference of the induced disturbances with normal skeletal growth and development must be considered

CHOICE OF EXPERIMENTAL ANIMAL

The adult laboratory rat was used in the present investigation mainly because in this species the minimal calcium need for equilibrium is well defined for different ages Furthermore in this species the adaptation to restricted calcium intake has been extensively studied by calcium balance techniques In principle the results of these studies agree with the observations made in humans (*Nicolaysen et al* 1953) The laboratory rat is further less liable to uncontrolled variation than man While in the rat the relation of different induced disturbances to the development of osteoporosis can be studied under well defined experimental conditions in man such possibilities are either restricted or non existent The fact that complete closure of *some of the epiphyseal zones* does not occur in the rat, does not necessarily mean that there is continued *active skeletal growth in the adult animal* Thus it has been reported that in the adult rat the epiphyseal cartilages are inactive (*El Maraghi et al* 1965) During the first 6 months of life calcification of bone is rapid and remains

steady thereafter (*Henry and Kon* 1953) Moreover, the uptake of radioactive calcium in bones of rats diminishes rapidly from the ages of 3 to 6 months and then decreases only little with age in accordance with measurements of growth rate determined by repeated labelling with tetracycline (*Bohr* 1968) Only rats stated to be 11½ to 12½ months old at the start of the experiment were used in the present investigation except for the animals of one special control group where older rats were used To ensure that the skeleton was fully mineralized at the start of the experiment all rats had been bred on an optimum intake of calcium and phosphorus *i e* 1 4 per cent Ca and 1 2 per cent P, and adequate amounts of vitamin D

PURPOSE OF THE INVESTIGATION

The aim of the present investigation was to determine in adult rats whether or not disturbances induced by a) prolonged calcium restriction and b) oophorectomy combined with prolonged prednisolone administration resulted in changes of the mature bone tissue and calcium metabolism which could be related to the development of osteoporosis according to the definition of *Albright and Reifenstein* (1948) Further the studies were planned with the purpose of following the sequence of changes in various parameters which could be related to the development of the disorder

The results reported herewith will concern the following specific relationships

I The effect of prolonged calcium restriction on the skeletal tissue of adult male rats

II The effect of prolonged calcium restriction on the blood calcium level and the distribution of Ca^{45} between blood and bone in adult male rats

III The effect of combined oophorectomy and prolonged prednisolone administration on the skeletal tissue of adult rats

IV The effect of combined oophorectomy and prolonged prednisolone administration on the blood calcium level and the distribution of Ca^{45} between blood and bone in adult rats

V The glycosaminoglycans of compact bone tissue in experimental osteoporosis induced by prednisolone treatment of oophorectomized rats or by calcium restriction

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Studies on the Development of Experimental Osteoporosis

I The Effect of Prolonged Calcium Restriction on the Skeletal Tissue of Adult Male Rats

by

Sven Erik Larsson

steady thereafter (*Henry and Kon* 1953) Moreover, the uptake of radioactive calcium in bones of rats diminishes rapidly from the ages of 3 to 6 months and then decreases only little with age in accordance with measurements of growth rate determined by repeated labelling with tetracycline (*Bohr* 1968) Only rats stated to be 11½ to 12½ months old at the start of the experiment were used in the present investigation except for the animals of one special control group where older rats were used To ensure that the skeleton was fully mineralized at the start of the experiment all rats had been bred on an optimum intake of calcium and phosphorus, *i e* 1 4 per cent Ca and 1 2 per cent P and adequate amounts of vitamin D

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ca'cium from the body but that they are able to maintain calcium equilibrium by increasing the uptake of dietary calcium from the intestine (*Hironaka et al* 1960)

Despite numerous studies on the adapta ion by the rat to a restricted calcium intake the reaction of the keleton to long term calcium deficiency is still poorly unders ood Young growing rats have been reported to develop osteoporosis on a diet deficient in calcium but adequate in vitamin D (*Crawford et al* 1957 *Harrison and Fraser* 1960) However it has also been reported that growing rats fed a similar diet deficient only in calcium develop skeletal changes typical of rickets (*Park et al* 1922 *Hess* 1929 *Engfeldt et al* 1962) The exper ments of *Gershon Cohen* et al (1962) suggest that a low calcium d et resul s in rachitic lesio s in the young growing rat but that in adults th condition is transformed in o osteoporo s A weaned rat placed on a low calcium diet shows signs of rickets for a short time only The rickets changes thereafter into osteoporosis without a change of diet (*McClendon and Blaustein* 1965)

The mature rat is genera'ly considered to be res s ent to the development of osteoporosis on re eiving a low calcium diet because of its effective adaptation to a low calcium intake It has been stated that a marked adaptation viz a distinctly increased efficiency of calcium absorption which compensates fully for any previous loss will occur only when the old rats have suffered a substantial lo s of calcium from the skeleton This delayed reaction might be expressed as a considerable period of latency In principle this finding agrees with observations in man (*Nicolaysen et al* 1953) However there appears to have been no previous investigation confined to a study of the effect of prolonged calcium deficiency on the skeleton of the adult rat and the pathomechanisms responsible for the skeletal changes induced by such treatment It was considered that such an investigation would provide valuable information concerning the relationship between calcium deficiency and the development of osteoporosis since the mechanisms involved in the adaptation to a restricted calcium intake seem to be similar for rats and humans

The present investigation was undertaken with the aim of studying the response of the mature skele al tissue to prolonged calcium restriction and of following the development of possible skeletal changes during *different periods* of maintained low calcium intake This report concerns the composition and the his o'ogy of the skeletal tissue in one year old male rats maintained on a low calcium diet for pe iods of time varying from 1 week up to 1 year

INTRODUCTION

The onset of generalized osteoporosis in humans has been related to a low intake or malabsorption of calcium (*Nordin* 1960, 1961, 1962 *Nordin et al* 1964 *Spencer et al* 1964) It has also been stated that in the generalized osteoporoses the bone mass is reduced because of the calcium needs of the organism (*Heaney* 1965) In human volunteers it has been shown by *Malm* (1958) that a negative calcium balance can be induced by changing from a normal to a low calcium intake In the great majority of the subjects, adaptation took place and the balance became less negative In a few subjects however there was a failure to adapt to the low calcium intake even after long periods of observation In these subjects the persisting negative calcium balance eventually resulted in osteoporosis

The relationship between calcium retention and body stores of calcium has been studied extensively in the rat In young growing animals a previous low intake of calcium increases the retention of calcium in a subsequent period on a high calcium diet (*Fairbanks and Mitchell* 1936 *Rottensten* 1938 *Nicolaysen* 1943, *Henry and Kon* 1947 and 1953) In old rats also the absorption of calcium has been found to be definitely increased after prolonged calcium restriction (*Henry and Kon* 1953 *Nicolaysen et al* 1953) However experiments by *Henry et al* (1960) indicated that old rats fed a low calcium diet need a minimum of 4 months to adapt themselves to the low calcium intake and that this period of adaptation is longer for old than for young rats In old rats a slow reduction of the absorption efficiency was observed by *Kane et al* (1949) while no change in the calcium metabolism with age was indicated by the findings of *Henry and Kon* (1953) and *Nicolaysen* (1956) *Hansard and Crowder* (1957) found that the true digestibility of dietary calcium by rats declined from 41 % at 48 to 72 weeks of age to 24 % at 106 weeks while the requirement for maintenance approximately doubled It has also been reported that aged rats (22 to 32 months compared to 10 to 12 months) are subject to a greater loss of

Chemical analyses showed that the diet contained 0.09 per cent Ca and 0.55 per cent P[1] The Ca P ratio was 1 6 1 The diet was supplied with an adequate amount of vitamin D All animals were given their diet and deionized water *ab libitum* The daily calcium intake was estimated at 18 20 mgs per animal Groups of 5 rats each were kept on this regimen for different periods of time in the short term series ten groups for 1 to 16 weeks and in the long term series six groups for 6 to 12 months In the short term series another group of 5 animals was fed the above described test diet supplemented with 4 % $CaCO_3$ this diet thus containing a total amount of 1 7 per cent Ca and 0 55 per cent P The Ca P ratio was 1 0 4 This diet and tap water were given *ab libitum* for 16 weeks and the daily calcium intake of these animals was estimated at 340—360 mgs

Control animals

In the short term series one group of 5 rats received a normal laboratory ration[2] containing 1 0 per cent Ca and 0 75 per cent P for 16 weeks The Ca P ratio was 1 0 75 Diet and tap water were given *ab libitum* The daily calcium intake of the rats belonging to this group was estimated at 200—220 mgs In the long term series one control group of 5 animals was fed the normal laboratory ration and tap water for 4 weeks in order to accustom the animals to the laboratory routine These animals were stated to be approximately 20 months old when delivered to the laboratory

Without access to direct sunlight all the animals were housed five to each cage at a temperature of 18—20°C The cages were large enough to allow the animals to move about freely No coprophagy was observed The series were planned so that all the animals within each series were sacrificed at the same time This was performed by bleeding them to death from the femoral artery under ether anaesthesia After sacrifice the animal bodies were kept in the deep freezer at – 20°C pending the subsequent preparations

Body weight

In all animals the initial and the final body weight was recorded In addition all the animals of the short term series were weighed weekly

[1] Here and in the following text the figures calculated on a dry weight basis are given

[2] Ewos Co Sodertalje Sweden

EXPERIMENTAL

A total number of 95 adult male rats of the Sprague Dawley strain[1] were divided into two experimental series Sixty animals comprised a short term and thirty five animals a long term series Apart from the duration of the test diet both series were treated identically All animals except the controls of the long term series (see page 21), were stated to 12 to 12 ½ months old at the start of the experiment The mean initial body weights of the animals of the two series were 499 0 ± 5 2 and 501 8 ± 9 2 grams respectively All animals had been bred on a standard laboratory ration containing on a dry weight basis, 1 4 per cent Ca and 1 2 per cent P and adequate amounts of vitamin D

Experimental animals

All the experimental animals were fed the low calcium diet of General Biochemical Inc Chagrin Falls, Ohio This diet has the following composition (GBI Bulletin D 15)

Ingredients	*Composition*
Whole Dried Egg (ether extracted)	27 0 %
Sucrose	10 0
Lard	10 0
Dried Yeast	7 0
Cod Liver Oil[2]	2 0
Starch	40 0
Salt mix	4 0
Salt mix	*Gms/100 lbs*
Ferric citrate	29 462
Magnesium chloride	855 122
Manganous sulfate	414
Potassium alum	190
Potassium chloride	355 491
Potassium citrate	371 976
Potassium iodide	085
Potassium sulfate	37 620
Sodium chloride	164 430
Sodium fluoride	1 048

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[1] Anticimex Co Stockholm

[2] Vitamin D_3 120 600 I U /100 g diet which was protected against daylight

Hydroxyproline determinations

The hydroxyproline content of the whole third metacarpal bone including bone marrow and articular cartilages was determined in both series by the method of *Neuman and Logan (1950)* The bone was carefully freed of soft tissues and periosteum All bones within each series were dried simultaneously at 48° C for 24 hours and were then weighed in weighing containers Protein hydrolysates were prepared by autoclaving the whole bone with 0 5 ml of 6 N hydrochloric acid in sealed tubes for 10 hours at 100° C A hydrolysis curve showed maximum hydroxyproline values after 6 hours and there was no decrease even after 21 hours hydrolysis Duplicate determinations were performed throughout and average values were used The coefficient of variation for these analyses was 2 0 per cent.

The gross bone density of the humerus

The density of the whole bone including bone marrow and articular cartilage, was determined according to *Robinson and Elliott* (1957) The right humerus of the animals of the two series was carefully dissected free from surrounding soft tissues and periosteum All bones within each series were soaked simultaneously in deionized water at 4 C for 16 hours Each bone was then suspended on a fine wire attached to the condyles and weighed while submerged in water at room temperature This was the weight of the hydrated whole bone submerged in water All bones of each series were then dried simultaneously at 105° C for 16 hours and using weighing containers the air dried weight was recorded The density of the dried whole bone was calculated by dividing the dry weight of the bone by the weight of water displaced by the dry bone volume

Preparation of undecalcified sections

The two proximal tail vertebrae of each animal of the long term series and one metacarpal bone from some of the animals of the short term series were freed of most of the surrounding soft tissues and then fixed and dehydrated in 6 changes of 96 per cent alcohol for 6 days The specimens were then placed in unpolymerized washed methyl methacrylate with the addition of a catalyst prepared as described by *Jousey et al* (1965) The specimens were embedded in glass bottles with semipolymerized monomer for one week and polymerization was then completed in an oven maintained at 37° C The glass bottle was then

Radiographs

At the start of the experiment each animal was examined radiologically under ether anaesthesia and at the end of the experiment this examination was repeated Each rat was placed with the spinal column and the extremities fixed directly on an X ray film and the same exposure conditions film and developer were used throughout

Measurement of the cortical thickness in the mid shaft of the femur

This examination was performed on all animals of the long term series The whole femur was dissected free from soft tissues and periosteum and its length from the top of the greater trochanter to the most distal point of the femoral condyles was measured with a caliper A fine bandsaw was then used to divide the bone in the middle ± 0 5 mm of the diaphysis perpendicularly to the long axis of the diaphysis With the aid of a caliper the internal and external transverse diameters were measured at the four cut surfaces obtained from the two divided femora of each animal The cortical thickness at this point was calculated as the difference between the external and internal diameters and with an accuracy of 0 05 mm Average values were used This figure was divided by the mean value for the external transverse diameter of the shaft at the same level and this fraction was multiplied by 100 In this way the femur score was calculated according to *Barnett and Nordin* (1960)

Ash determinations

The ash content of the whole tibia including bone marrow and articular cartilages was determined in both experimental series as follows After careful dissection from soft tissues and periosteum the bone was placed in a weighing container and the wet weight was immediately recorded in a *Mettler* balance with an accuracy of 0 05 mg All bones within each series were thereupon ashed simultaneously in a muffle furnace at 700°C for 16 hours and the weight of the ashes was then recorded The ash content was expressed as per cent of the wet weight In the short term series the ash contents of both tibiae were determined and average values recorded As no statistically significant difference between the ash contents of the right and the left tibiae was found only the right tibia was used in the long term series

PW 1009 apparatus provided with a copper anode and a nickel window the X ray tube operating with 20 kV and 20 mA. After an exposure time of 15 minutes the plates were developed for five minutes in Kodak D 158 washed and fixed in a conventional acid fixative Longitudinal sections of metacarpal bones in the short term series were ground first on an oscillating grinder then by hand and microradiographs were prepared as described above

Preparation of decalcified sections

The fourth metacarpal bone of all the rats of the short term series and the third tail vertebra of those of the long term series were fixed in 10 per cent neutral formaldehyde for 24 hours and then decalcified for 12 14 days in a mixture of equal parts of monosodium citrate (20 %) and formic acid (44 %) The specimens were then immersed in 5 per cent disodium sulphate for twenty four hours washed with water for twenty four hours and dehydrated by successively immersing in 70 95 per cent and absolute alcohol (2 changes) Finally the specimens were immersed first in methyl benzoate and then in xylol and embedded in paraffin Five μ thick longitudinal sections of the metacarpal bones and cross sections of the vertebrae were cut and stained with Ehrlich s haematoxylin and eosin and in addition, with azocarmine G Sections from the vertebrae were also stained with an 0 5 per cent solution of toluidine blue in phthalate at pH 4 4 as described by *Belanger and Hartnett* (1960)

Statistical treatment of data

For the computation an analysis of variance with one way lay out according to *Scheffe* (1961) was used The hypothesis of no difference between groups was tested with a 5 per cent significance level Significant contrasts between groups were tested at the same significance level according to *Scheffe* (1961) For computation of the data obtained from the one group fed the test diet enriched with calcium Student s t test was used according to *Brownlee* (1965) and with a significance level of 5 per cent[1]

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[1] In the following text the term significant" will stand for statistically significant

broken and the excess methacrylate was trimmed off with a bandsaw For the subsequent examinations of the vertebrae, the plastic blocks were sawn into slices approximately 0 5 mm thick and exactly perpendicular to the long axis of the vertebra while the metacarpal bones were ground directly as described below

Tetracycline labelling

All animals of the long term series were labelled with chlortetracycline (Aureomycin© Lederle) in two doses of 20 mg per kg body weight administered by intraperitoneal injection 10 and 20 days before sacrifice Approximately 60 μ thick undecalcified methacrylate embedded cross sections from the second tail vertebra were mounted under coverslips in fluorescence free balsam (Permount) and examined in a Zeiss fluorescence microscope fitted with an UV light source (High Pressure Vacuum lamp HBO 200, exciter filters UG 2 and UG 5, barrier filters 65 and 41)

Quantitation of the amount of vertebral bone

Quantitation of the amount of bone present in a standard area was performed in the long term series as follows Undecalcified sections embedded in methacrylate from the first tail vertebra were ground first on an oscillating grinder then by hand to a thickness of approximately 50 μ Only sections containing most of the transverse processes were studied these were examined unstained with the aid of an integrating eye piece (Zeiss I) as described by Wagner (1965) The number of vertebral bone hits of 200 points was determined with the point network exactly in the centre of the section at a linear magnification of 30 x the accuracy was found to be more than 95 per cent

Microradiographs

Microradiographs were prepared from the animals of the long term series as follows Undecalcified cross sections embedded in methacrylate from the second tail vertebra were ground on a Knuth Rotor grinder to a thickness of approximately 60 μ Silicon Carbide papers Nos 220 and 600 and water as a lubricant being used The sections were then placed in direct contact with a fine grain emulsion (Kodak MR plates) and were radiographed in a Philips

Groups	Initial body weight grams	S E M	Final body weight grams	S E M	Difference in % of the initial body weight	S E M
Normal laboratory ration for 16 weeks	454 0	7 6	502 0	16 9	13 5	1 0
long term series	453 0	13 5	466 3	13 0	3 0	0 4
Low cal ium diet for 1 week	503 4	11 8	521 4	12 6	3 6	0 1
2 weeks	510 2	9 2	536 2	10 5	5 1	0 5
3	470 3	5 1	510 9	12 6	8 6	1 8
4	482 3	4 6	522 6	10 2	8 5	1 3
5	532 4	9 3	562 4	11 6	5 6	0 8
8	504 7	6 6	544 1	8 5	7 8	1 6
10	529 6	11 8	578 6	9 3	9 4	1 6
12	529 8	18 8	608 1	23 7	14 8	0 9
14	476 7	13 6	595 3	10 8	25 1	2 5
16	469 0	14 1	610 5	15 4	30 1	0 9
6 months	501 3	11 5	510 0	13 0	1 8	1 6
7	577 9	8 1	567 2	21 0	-1 4	2 5
8	534 4	7 6	550 5	22 4	3 8	3 2
9	522 6	32 6	525 9	24 1	1 8	6 7
10	452 8	9 3	540 4	27 6	20 7	3 7
12	484 7	18 7	562 2	51 5	15 3	7 1
Calcium enriched diet for *16 weeks*	482 6	13 4	576 9	22 6	19 2	2 0

Table 1 a The initial and final body weights of the rats fed the normal laboratory ration the low calcium diet and the calcium enri hed diet
(S E M =standard error of the mean)

Six deaths occurred among the whole material five among the experimental animals in the long term series and one in the short term series all probably due to advanced age These animals were excluded The remaining animals were in good health

Body weights (Fig 1 Table 1 a b)

The rats fed the normal laboratory ration increased their body weight by almost 10 per cent during the first 7 weeks of observation From then on and until the 16th week the body weight remained unchanged In the animals fed the low calcium diet the body weight increased by almost 30 per cent during the first 7 weeks Subsequently and up to the end of the 16th week no significant change was noted The animals fed the low calcium test diet supplemented with

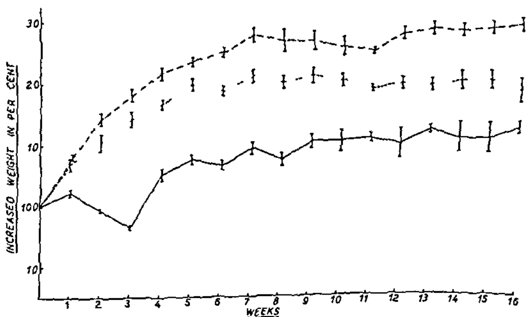


Fig 1 Body weight change in per cent of the initial weight in the three groups of rats fed the normal laboratory ration (uninterrupted line) the low calcium diet (broken dotted line) and the calcium enriched diet (broken line) for 16 weeks The bars represent the standard error of the mean

Femur length

The femur length in the long term series showed no significant difference between the control group and the groups of animals fed the low calcium diet.

Radiographs

Radiological examination revealed that the epiphyseal zones of the long bones were closed in all animals In some animals distributed at random among the whole material the remnants of the epiphyseal zones were recognized as a sclerotic line In none of the animals maintained on a low calcium diet for 1 to 16 weeks was any notable change observed on radiographs taken at the start and at the end of the experimental period On the other hand all animals fed the low calcium diet for 6 months and longer showed a slight but definite reduction of the cortical thickness of the tubular bones and the pelvis and decreased density of the trabecular pattern in the metaphyses and in the tail vertebrae

The cortical thickness in the mid shaft of the femur (Table 2)

Direct measurement of the cortical thickness was performed in the long term series and revealed significantly lower values for the femur score" in all the six groups of rats fed the low calcium diet for 6 to 12 months compared with the control group The lower values for the cortical thickness corresponded to higher values for the internal transverse diameter while the external diameter showed no significant difference

The ash content of the whole tibia (Fig 2 Table 3)

The ash contents of the tibiae of the rats fed the low calcium diet for 1 to 12 weeks showed no significant difference from those of the rats fed the normal laboratory ration Significantly lower values decreasing with time were obtained in the eight groups of rats kept on a low calcium intake for 14 weeks to one year The decrease amounted to 6 2 % after 16 weeks of calcium restriction and 13 3 % after 12 months The group of rats fed the diet enriched with calcium for 16 weeks showed slightly higher values than those of the group fed the normal laboratory ration for 16 weeks This difference was not significant

calcium showed an increase in their initial body weight by *approximately 20 per cent* during the first 5 weeks from that time onwards and until the end of the 16th week it remained unchanged (Fig 1) All rats given the test diet showed an appreciable increase in their subcutaneous and peritoneal fat tissue This was more pronounced in the animals fed the low calcium diet than in those for which this diet was enriched with calcium The final body weight showed no significant difference in the groups of rats fed the low calcium diet for 5 weeks up to 1 year (Table 1 a, b)

Weeks	Normal laboratory ration Body weight change %	S E M	Low calcium diet Body weight change %	S E M	Calcium enriched diet Body weight change %	S E M
1	2 5	0 63	8 4	0 64	7 1	1 13
2	-1 3	0 32	14 4	1 11	10 7	1 40
3	-3 4	0 67	18 6	1 13	14 5	1 36
4	5 5	1 11	21 9	0 99	17 2	0 88
5	7 9	0 80	24 2	0 69	20 2	0 97
6	7 0	0 70	25 6	0 83	19 2	0 75
7	9 9	1 18	28 4	1 31	21 7	1 08
8	7 7	0 99	27 6	1 75	20 6	1 04
9	10 7	1 74	27 7	1 49	21 7	1 36
10	11 0	1 85	26 6	1 63	21 1	0 94
11	11 4	0 71	26 1	0 60	19 8	0 61
12	10 5	2 72	28 7	1 13	20 4	1 01
13	13 0	0 64	29 4	1 04	20 3	0 96
14	11 6	2 77	29 2	1 04	21 0	1 50
15	11 3	2 83	29 5	0 94	20 8	1 48
16	13 4	0 97	30 1	0 92	19 2	2 00
	F = 9 91 sign		F = 29 54 sign		F = 12 12 sign	

$F_{0\,95}$ (15 61) = 1 85 $\quad$ $F_{0\,95}$ (15 64) = 1 84

Table 1 b Body weight change in per cent of the initial weight in the three groups of rats fed the normal laboratory ration the low calcium diet and the calcium enriched diet for 16 weeks

Femur length

The femur length in the long term series showed no significant difference between the control group and the groups of animals fed the low calcium diet.

Radiographs

Radiological examination revealed that the epiphyseal zones of the long bones were closed in all animals In some animals distributed at random among the whole material the remnants of the epiphyseal zones were recognized as a sclerotic line In none of the animals maintained on a low calcium diet for 1 to 16 weeks was any notable change observed on radiographs taken at the start and at the end of the experimental period On the other hand all animals fed the low calcium diet for 6 months and longer showed a slight but definite reduction of the cortical thickness of the tubular bones and the pelvis and decreased density of the trabecular pattern in the metaphyses and in the tail vertebrae

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Groups	No of animals	External diameter mm	S E M	Internal diameter mm	S E M	Femur score	S E M
Normal laboratory ration	5	5 10	0 03	2 69	0 02	47 7	0 29
Low calcium diet for 6 months	4	5 11	0 07	3 29	0 19	35 7	3 51
7	4	5 41	0 02	4 01	0 10	25 9	2 11
8	3	5 13	0 09	3 40	0 16	33 7	3 57
, 9 ,	5	5 21	0 10	3 66	0 22	30 0	3 06
10 ,	5	5 20	0 09	3 59	0 17	30 8	3 51
, 12	4	5 06	0 13	3 63	0 15	28 3	3 48
		Γ = 1 81 n s		F = 7 04 sign		Γ = 6 54 sign	
				$\Gamma_{0 \jmath}$ (6 23) = 2 58			

Table 2 The external and internal transverse diameter at the mid shaft of the femur and the femur score in rats fed the normal laboratory ration and the low calcium diet

however Similar values were obtained for the control group of the short term and the long term series

The hydroxyproline content of the whole metacarpal bone (Fig 3 Table 4)

The hydroxyproline content of the whole metacarpal bone of the rats fed the low calcium diet for 1 to 10 weeks showed no significant differences compared with those of the group fed the normal laboratory ration Significantly lower

Groups		No of animals	% ash	S E M	
Normal laboratory ration		10	48 2	0 31	
Low calcium diet for	1 week	4	48 0	0 48	
	2 weeks	5	47 7	0 25	
	3	5	47 4	0 46	
	4	5	45 5	0 52	
	5	5	47 1	1 00	
	8	5	46 6	0 68	
	10	5	47 8	0 20	
	12	5	47 6	0 42	
	14	5	45 3	0 28	}
	16	5	45 2	0 43	}
	6 months	4	44 9	0 96	}
	7	4	44 5	0 17	}
	8	3	44 4	0 61	} sign
	9	5	43 6	0 82	}
	10	5	43 3	1 08	}
	12	4	41 8	1 80	}
			F = 7 89 sign		
			$F_{0.05}$ (16 67) = 1 82		
Calcium enriched diet for 16 weeks		5	48 8	0 45	n s

Table 3 The percentage ash content of the whole tibia in rats fed the normal laboratory ration the low calcium diet and the calcium enriched diet.

ASH
TIBIA
50 0
45 0
40 0
LOW CALCIUM DIET
NORMALS
DIET + C
0 1 2 3 4 5 6 7 8 9 10 11 12
MONTHS
TEST VARIABLE F = 7 89
$F_{0\ 95}(16\ 67) = 1\ 82$

Fig 2 The percentage ash content of the tibia in rats fed the normal laboratory ration the low calcium diet and the calcium enriched diet

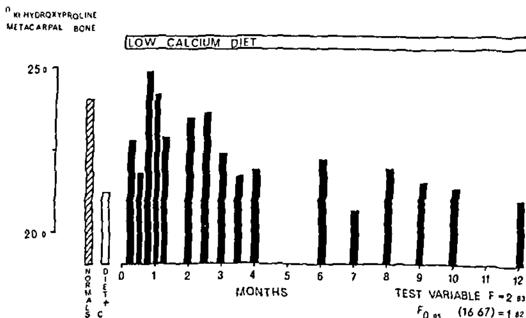


Fig 3 The promille hydroxyproline content of the metacarpal bone in rats fed the normal laboratory ration the low calcium diet and the calcium enriched diet

values were obtained in the nine groups of rats fed the low calcium diet for 12 weeks to 12 months than in the normal controls The group of rats fed the calcium enriched diet for 16 weeks showed slightly lower values than the group fed the normal laboratory ration This difference was significant. Comparison between the two control groups showed no significant difference

Groups		No of animals	‰ hydroxy proline	S E M	
Normal laboratory ration		10	24 1	0 39	
Low calcium diet for	1 week	4	22 8	0 71	
	2 weeks	5	21 8	0 43	
	3	5	24 9	1 11	
	4	5	24 2	1 06	
	5	5	22 9	0 64	
	8	5	23 5	0 93	
	10	5	23 7	0 81	
	12	5	22 4	0 72	sign
	14	5	21 7	0 66	sign
	16	5	21 9	0 84	sign
	6 months	4	22 3	0 52	sign
	7	4	20 7	0 56	sign
	8	3	22 0	0 75	sign
	9	5	21 6	0 76	sign
	10	5	21 4	0 51	sign
	12	4	21 0	0 69	sign
			$F = 2\ 83$ sign.		
			$F_{0\ 01}\ (16\ 67) = 1\ 82$		
Calcium enriched diet for 16 weeks		5	21 2	0 86	sign

Table 4 The promille hydroxyproline content of the metacarpal bone in rats fed the normal laboratory ration the low calcium diet and the calcium enriched diet.

ASH TIBIA

LOW CALCIUM DIET

50 0 — 45 0 — 40 0

NORMALS DIET + C 0 1 2 3 4 5 6 7 8 9 10 11 12

MONTHS

TEST VARIABLE $F = 7\ 89$

$F_{0\ 95}(16\ 67) = 1\ 82$

Fig 2 The percentage ash content of the tibia in rats fed the normal laboratory ration the low calcium diet and the calcium enriched diet

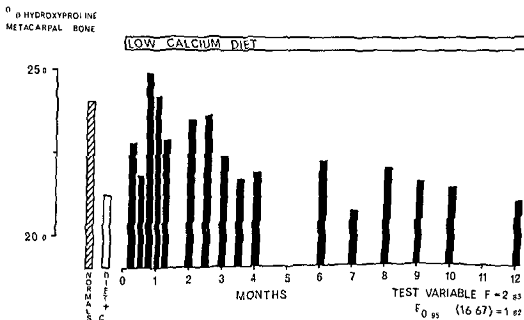


Fig 3 The promille hydroxyproline content of the metacarpal bone in rats fed the normal laboratory ration the low calcium diet and the calcium enriched diet

values were obtained in the nine groups of rats fed the low calcium diet for 12 weeks to 12 months than in the normal controls The group of rats fed the calcium enriched diet for 16 weeks showed slightly lower values than the group fed the normal laboratory ration This difference was significant Comparison between the two control groups showed no significant difference

Groups		No of animals	°/₀₀ hydroxy proline	S E M	
Normal laboratory ration		10	24 1	0 39	
Low calcium diet for	1 week	4	22 8	0 71	
	2 weeks	5	21 8	0 43	
	3	5	24 9	1 11	
	4	5	24 2	1 06	
	5	5	22 9	0 64	
	8	5	23 5	0 93	
	10	5	23 7	0 81	
	12	5	22 4	0 72	sign
	14	5	21 7	0 66	sign
	16	5	21 9	0 84	sign
	6 months	4	22 3	0 52	sign
	7	4	20 7	0.56	sign
	8	3	22 0	0 75	sign
	" 9	5	21 6	0 76	sign
	10	5	21 4	0 51	sign
	12	4	21 0	0 69	sign
			$F = 2\ 83$ sign		
			$F_{0.05}\ (16\ 67) = 1\ 82$		
Calcium enriched diet for 16 weeks		5	21 2	0 86	sign

Table 4 The promille hydroxyproline content of the metacarpal bone in rats fed the normal laboratory ration the low calcium diet and the calcium enriched diet

ASH
TIBIA
50 0
45 0
40 0
LOW CALCIUM DIET
NORMALS
DIET + Ca
0 1 2 3 4 5 6 7 8 9 10 11 12
MONTHS
TEST VARIABLE F = 7 89
$F_{0\ 95}(16\ 67) = 1\ 82$

Fig 2 The percentage ash content of the tibia in rats fed the normal laboratory ration, the low calcium diet and the calcium enriched diet

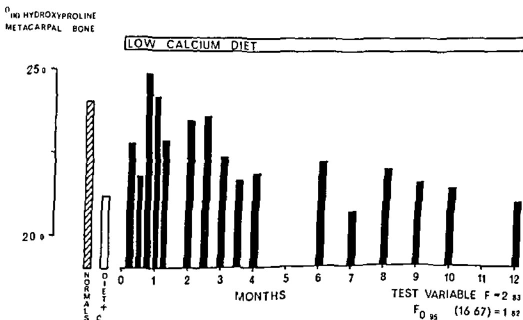


Fig 3 The promille hydroxyproline content of the metacarpal bone in rats fed the normal laboratory ration the low calcium diet and the calcium enriched diet

Groups	No of animals	Density	S E M	
Normal laboratory ration	10	2 28	0 016	
Low calcium diet for 1 week	4	2 30	0 023	
2 weeks	5	2 30	0 032	
3	5	2 29	0 039	
4	5	2 28	0 025	
5	5	2 31	0 023	
8	5	2 27	0 022	
10	5	2 26	0 016	
12	5	2 26	0 017	
14	5	2 27	0 005	
16	5	2 31	0 015	
6 months	4	2 11	0 013	sign
7	4	2 05	0 048	sign
8	3	2 09	0 038	sign
9	5	2 09	0 039	sign
10	5	2 11	0 046	sign
12	4	2 07	0 049	sign
		$\Gamma = 10\ 90$ sign		
		$\Gamma_0 \quad (16\ 67) = 1\ 82$		
Calcium enriched diet for 16 weeks	5	2 37	0 014	sign

Table 5 The gross bone density of the humerus in rats fed the normal laboratory ration the low cal ium diet and the calcium enriched diet

The percentage of vertebral bone hits (Table 6)

This was examined in the long term series The six groups of animals maintained on a low calcium diet for 6 to 12 months showed significantly lower values than the control group

Microradiography

Microradiographs of undecal ified vertebral cross sections showed that in the normal control rats the cortical and trabecular bone was quite evenly mineralized

The gross bone density of the humerus (Fig 4, Table 5)

The values obtained from the rats fed the low calcium diet for 1 to 16 weeks showed no consistent changes with time during the period of restricted calcium intake, but only a small intergroup variation and the statistical analysis revealed no significant differences The six groups of rats kept on a restricted calcium intake for 6 to 12 months showed significantly lower values than the normal controls The group of rats fed the calcium enriched diet for 16 weeks showed slightly higher values than the groups fed the normal laboratory ration This difference was significant Similar values were obtained for the two control groups

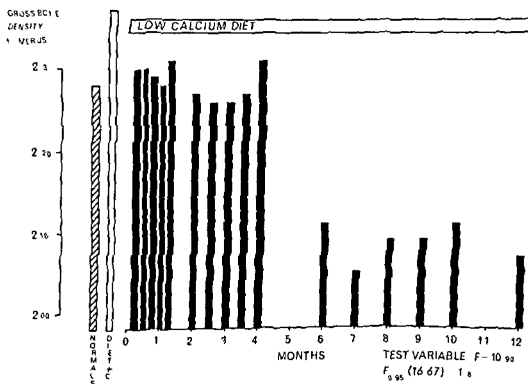


Fig 4 The gross bone density of the humerus in rats fed the normal laboratory ration the low calcium diet and the calcium enriched diet

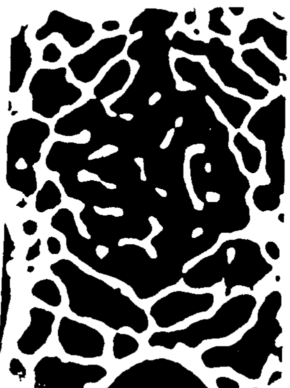


Fig. 5 Microradiograph of a cross section through the second tail vertebra of a normal rat. The bone is evenly mineralized (x 25)



Fig. 6 Microradiograph of a cross section through a corresponding part of the second tail vertebra of a rat fed the low calcium diet for 12 months (x 25)

Groups	No of animals	% hits	S E M	
Normal laboratory ration	5	46 9	1 68	
Low calcium diet for 6 months	4	36 2	1 92	
, ,, ,, ,, 7 ,,	4	32 5	1 32	
,, , ,, 8 ,,	3	35 2	0 44	sign
, , ,, ,, 9 ,,	5	36 7	2 80	
, ,, 10 ,	5	37 7	0 88	
, , ,, 12 ,	4	31 5	4 04	
		F = 5 46 sign		
		$F_{0 05}$ (6 23) = 2 53		

Table 6 The vertebral bone mass calculated as percentage bone hits in rats fed the normal laboratory ration and the low calcium diet

(Fig 5) The bone had a non lamellar (woven) appearance as described by *Enlow (1963)* No secondary osteones or resorption cavities were observed In the animals maintained on a low calcium intake for 6 to 12 months the microradiographs had a similar appearance to those in the control group with the exception that the bone trabeculae were considerably thinner (Figs 6 and 7) There was no difference in the degree of mineralization and both the cortical and the trabecular bone were as evenly mineralized as in the control animals No resorption cavities were found Microradiographs from longitudinal sections of the metacarpal bone in the short term series showed that the bone was evenly mineralized and that the epiphyseal zones were closed

Histological observations

In the short term series decalcified longitudinal sections from the metacarpal bone of each animal were stained with haematoxylin eosin and azocarmine G respectively In all the animals the epiphyseal zones were closed The sections stained with haematoxylin eosin showed that in the control group the diaphysis contained mostly small osteocytes Osteocytes with enlarged spherical lacunae were located approximately midway between the border of the central marrow cavity and the periosteum Occasionally the lacunae in that area were empty

no change in the staining properties was observed The slightly basophilic areas did not differ from those in the control animals The osteoid tissue was very scanty in the normal animals No increase in the amount of osteoid tissue was observed in the calcium deficient animals Neither was any difference observed in the amount of fibrous tissue associated with bone

In the long term series decalcified cross sections of the vertebrae were stained with toluidine blue at pH 4 4 and in addition with haematoxylin-eosin and azocarmine G In the different animals sections were cut from parts of the vertebra chosen at random In each animal all the sections were cut from the same part of the vertebra allowing adjacent sections to be examined after different staining procedures The cortical bone contained mostly small osteocytes but larger osteocytes were also found especially midway between the marrow cavity and the periosteum The trabecular bone also contained small osteocytes and occasionally slightly larger ones The cytoplasm the immediate border of

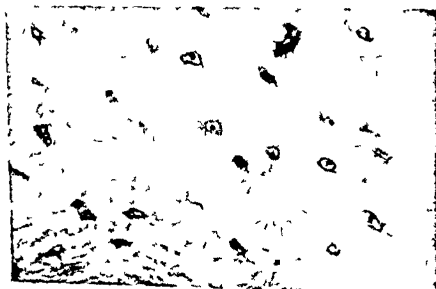


Fig 8 Photomicrograph of vertebral cortical bone from a normal adult rat A variety of osteocytes and also empty lacunae can be seen Haematoxylin eosin (x5 [illegible])



Fig. 7 A detail of the microradiograph shown in fig 6 The bone is evenly mineralized and there is no difference from normal in the degree of mineralization of the remaining bone tissue (x 100)

of cells and had become filled with an amorphous substance The immediate border of the osteocyte lacunae and the processes of the osteocytes were slightly basophilic In the metaphyseal bone trabeculae slightly basophilic areas were seen These areas were located either centrally or peripherally in a trabecula and frequently extended to its surface Occasionally small scattered irregular areas which were slightly basophilic were observed in the cortex

Histological sections from rats fed the low calcium diet for 1 to 16 weeks showed a similar appearance to those from the normal control animals In all sections osteoblasts and osteoclasts were scanty In fact no osteoclasts were observed either in the normal controls or in the animals fed the low calcium diet The osteocytes had the same appearance as in the control animals and



Fig 12 Photomicrograph of ertebral bone from a rat fed the low calcium diet for 9 months Bone trabeculae with slightly basophilic areas. Haema toxylin eosin. (x125)



Fig 13 Photomicrograph of an adjacent section of the vertebral bone shown in fig 12 Small areas staining only light, or not at all located between the dark staining collagen bundles Azocarmine G (x125)



Fig 14 Photomicrograph of an adjacent ection of the ertebral bone shown in fig 12 and 13 The areas described in fi 12 and 13 show an intense metachromasia No difference in the staining properties of these areas was observed between normal rats and rats fed the low calcium diet for 6 to 12 months Toluidine blue at pH 4 4 (x125)

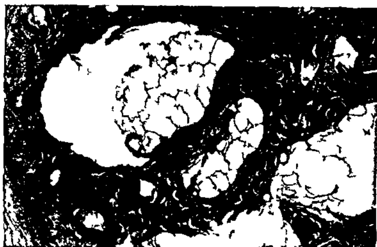


Fig 9 Photomicrograph of vertebral bone from a normal rat showing slightly basophilic areas Haematoxylin eosin (x125)

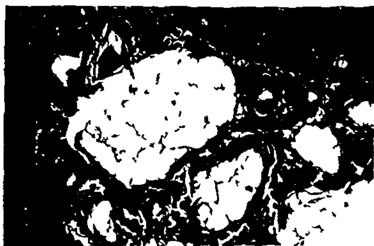


Fig 10 Photomicrograph of an adjacent section of the vertebral bone shown in fig 9 Between the dark staining collagen bundles light areas con be observed Azocarmine G (x125)

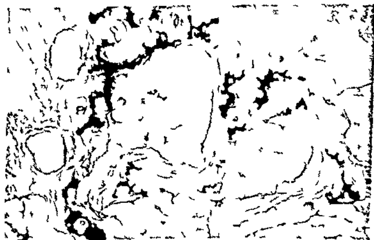


Fig 11 Photomicrograph of an adjacent section of the vertebral bone shown *in fig 9 and 10* Areas which stained slightly basophilic with haematoxylin eosin and light or not at all with azocarmine G show an evident metachromasia Toluidine blue at pH 4 4 (x125)



Fig 12 Photomicrograph of vertebral bone from a rat fed the low calcium diet for 9 months Bone trabeculae with slightly basophilic areas Haematoxylin eosin (x125)



Fig 13 Photomicrograph of an adjacent section of the vertebral bone shown in fig 12 Small areas staining only light, or not at all located between the dark staining collagen bundles Azocarmine G (x125)



Fig 14 Photomicrograph of an adjacent section of the vertebral bone shown in fig 12 and 13 The areas described in fig 12 and 13 show an intense metachromasia. No difference in the staining properties of these areas was observed between normal rats and rats fed the low calcium diet for 6 to 12 months Toluidine blue at pH 4 4 (x125)

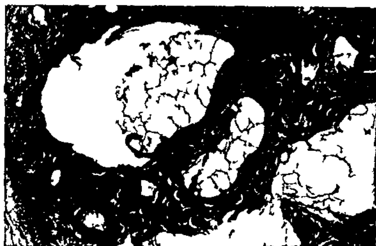


Fig 9 Photomicrograph of vertebral bone from a normal rat showing slightly basophilic areas Haematoxylin eosin (x125)

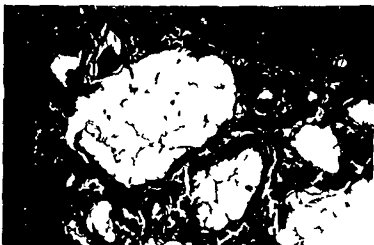


Fig 10 Photomicrograph of an adjacent section of the vertebral bone shown in fig 9 Between the dark staining collagen bundles light areas con be observed Azocarmine G (x125)



Fig 11 Photomicrograph of an adjacent section of the vertebral bone shown in fig 9 and 10 Areas which stained slightly basophilic with haematoxylin eosin and light or not at all with azocarmine G show an evident metachromasia Toluidine blue at pH 4 4 (x125)

areas were located in the trabecular bone and were observed most frequently in the metaphyseal regions Nearer the mid portion of the vertebra the basophilic areas decreased in frequency The basophilic areas were located in the spaces intervening between parallel fibered bone (Fig 10) and were metachromatic with toluidine blue (Fig 11) No difference in the staining properties of these areas was observed between normal animals and osteoporotic animals fed the low calcium diet for 6 to 12 months (Figs 12—14)

Fluorescence microscopy

In the normal animals fluorescence of newly formed bone was observed mainly on the trabecular surfaces (Fig 15) and on the surfaces of bone canals Only parts of the trabecular surfaces were fluorescent while others were not Despite the time interval of 10 days between the two administered doses there was as a rule only one fluorescent line to be observed Occasionally double



Fig 16. Fl orophotomi rograph showing labell ng of a vertebral bone trabecula in a at fed the l w calc m d et for 9 mor ths. The *labelling is similar* to that in the normal rat (x4)

the osteocyte lacunae and the processes of the osteocytes were slightly basophilic with haematoxylin eosin and metachromatic with toluidine blue Lacunae empty of cells were occasionally found especially in the cortical bone (Fig 8) Some of these lacunae were filled with an amorphous substance which was metachromatic with toluidine blue stain The osteocytes and the lacunae had a similar appearance in normal and experimental animals The frequency of osteoblasts and osteoclasts was very low in the normal control animals and no increase was found in the calcium deficient osteoporotic animals The sections stained with haematoxylin eosin or azocarmine G showed that the amount of osteoid tissue in the control animals was very small No increase of the osteoid tissue was observed in the animals maintained on a prolonged low calcium diet As in the tubular bone, areas which showed slightly basophilic staining with haematoxylin eosin were also found in the vertebral sections (Fig 9) These



Fig 15 Fluorophotomicrograph showing labelling of a vertebral bone trabecula in a normal rat Despite the time interval of 10 days between the two administered doses of chlortetracycline there is only one fluorescent line indicating a relatively low rate of new bone formation (x400)

rats kept on a low calcium intake were given a diet containing 0 09 per cent calcium and adequate amounts of phosphorus and vitamin D The prevailing experimental conditions were therefore sufficient to bring the animals into a negative calcium balance In a negative calcium balance the difference between calcium intake and output is evidently taken from the skeleton In the ten groups of animals maintained on a low calcium intake for 1 to 16 weeks no change was observed in the roentgenological appearance of the skeleton and the density of the whole bone Neither the *hydroxyproline* content nor the ash content of whole bones showed any significant changes during the first 12 and 14 weeks of calcium restriction Not until after 14 weeks on a restricted calcium intake was a definite reduction in bone mass, *i e* a reduction of both the mineral and organic components as determined by the measurement of the contents of ash and hydroxyproline of whole bones observed in the old rats used in the present study This finding supports the observations by *Henry et al.* (1960) that old rats kept on a similar low calcium diet remain in negative calcium balance for at least 4 months In the present study a reduction of both the trabecular and the cortical bone resulting in a decrease in the density of the whole bone was found on X ray examination by direct measurement of the cortical thickness in the mid shaft of the femur, *i e* femur score" and in the percentage of vertebral bone hits" The reduction in the ash and the hydroxyproline contents of whole bones indicates a concomitant reduction of both the mineral and the collagen component of the skeletal tissue Thus during the long term negative calcium balance induced by a restricted calcium intake in this experiment, mobilization of skeletal cal ium occurred with a concomitant breakdown of organ c bone ma rix

The bone composition of the rats in the group fed the test diet enriched with calcium for 16 weeks suggests an increase in the degree of mineralization compared with that of the animals fed the normal laboratory ration for the same period of time Thus there was a significant increase in gross bone density compared with that of the normal controls The observed increased ash content together with a decrease in the percentage hydroxyproline content of whole bones suggests an increased degree of mineralization of the bone collagen This is further supported by the decreased retention of intraperitoneally administered Ca^{45} found in the same animals in a subsequent study (*Larsson* 1969)

It has been suggested from observations made in calcium balance studies on old rats that a considerable calcium deprivation by 5 per cent or more of the total body calcium is followed by a distinct, compensatory increase of the calcium absorption which continues with high efficiency until the total loss

fluorescent lines were found The distance between the lines was *quite short*, indicating a relatively low rate of new bone formation

In the osteoporotic animals fed the low calcium diet for 6 to 12 months the tetracycline fluorescent micrographs had a similar appearance to *those in the* normal control animals (Fig 16) No difference in the degree of trabecular labelling was observed Only occasionally were double fluorescent lines found and the distance between the lines was not apparently different from that in the *control animals* The bone canals showed the same degree of labelling as in the normal rats Both in the normal and in the calcium deficient rats the fluorescent uptake was highest in the metaphyseal regions of the vertebra

DISCUSSION

The present study is concerned with the reaction of the well mineralized skeleton of one year old fully grown rats to a restricted calcium intake The preliminary feeding induces different degrees of saturation of the calcium stores (*Fairbanks and Mitchell 1936*) and a normal calcium intake is necessary for the growth of all the tissues including bone whether other conditions necessary for calcification are present or not (*Carttar et al 1950 Toothill and Hosking 1968*) The animals used in the present investigation had been bred on an optimum intake of calcium phosphorus and vitamin D and rats with a mature skeleton were used in order to eliminate the interference of skeletal growth with the skeletal response of the treatment The fact that the body weight of the control animals remained almost unchanged during the period of observation in combination with the absence of any difference in length of the bones strongly suggests that the skeletal growth of the animals used was completed at the start of the experiment This is further supported by the observation that the uptake of radioactive calcium in bones of rats diminishes rapidly from the age of 3 to 6 months and then decreases very little with age in accordance with the growth rate (*Bohr* 1968) By histological examination it has been found that the epiphyseal cartilages are inactive in aged rats (*El Maraghi et al* 1965) This observation was confirmed by the examinations performed in the present study

Old rats need approximately 0 5 per cent calcium in the diet to maintain calcium equilibrium (*Henry and Kon* 1947) In the present investigation the

showing basophilia with haematoxylin eosin are normally present in the metaphyseal bone in the rat some investigators have recognized the association of similar areas with resorption (*Ruth* 1954 1961) Also in the old rats used in the present investigation basophilic areas were found in the bone trabeculae of the metaphysis of the vertebrae Examination of decalcified sections stained with haematoxylin eosin azocarmine G or toluidine blue at pH 4 4 indicated that these areas consisted of intercellular substance probably containing acid mucopolysaccharides extending from the epiphysis into the bone trabeculae The staining properties of these areas were similar in osteoporotic animals and normal controls No changes were observed which could be related to the osteoporotic process Intensified staining of mucopolysaccharides has been reported in areas where bone removal is taking place (*Heller Steinberg* 1951 *Engel* 1952) While in those experiments young growing animals were studied under conditions of induced rapid bone resorption no such changes were observed in the adult animals used in the present investigation

Osteolysis *i e* osteocytic resorption of cells surrounded by matrix that contains mucopolysaccharides and induces toluidine blue metachromasia has been observed after the institution of low calcium or high phosphorus diets (*Belanger* 1965) Osteoclastic resorption has been considered to be of far less importance than osteolysis in both normal bone remodelling and in accelerated resorption as *e g* *in hyperparathyroidism* (*Belanger et al* 1963 *Belanger and Robichon* 1964 *Gries* 1966 *Brown et al* 1966) In the present investigation no increase in metachromasia around osteocytes was observed in the calcium deficient osteoporotic animals compared with the normal controls The appearance of increased osteolysis is probably dependent upon the degree of calcium deficiency induced

While young rats are reported to develop skeletal changes typical of rickets upon specific calcium deficiency (*Park et al* 1922 *Hess* 1929 *Carttar et al* 1950 *Engfeldt et al* 1962 *Gershon Cohen et al* 1962 *McClendon and Blaustein* 1965) no signs of rickets or osteomalacia were found at any stage of calcium deficiency by the histological microradiographical and tetracycline labelling studies performed in the present investigation Osteoporotic bone changes reported in young calcium deficient rats by *Crawford et al* (1957) and *Harrison and Fraser* (1960) are apparently late changes secondary to calcium-deficiency rickets and disturbed skeletal growth (*Gershon Cohen et al* 1962 *McClendon and Blaustein* 1965) No conclusions can be drawn from those experiments regarding the maintenance of the mature skeleton and the development of osteoporosis which characteristically is a disease of the adult individual

in the calcium deprivation period has been compensated (*Nicolaysen et al* 1953). In the present investigation the maximum decrease in the ash content of the whole bone amounted to 13 3 per cent and was found in the group of rats maintained on a low calcium intake for 12 months After the 14th week of restricted calcium intake there was a successive reduction in the ash content of the tibia This finding is not consistent with a delayed increase in calcium absorption and calcium equilibrium despite continuous low calcium intake A further reduction in bone mass would not have been expected otherwise in the groups of rats kept on the low calcium diet for the longer periods of time i e 10 to 12 months It is thus, of great interest that, contrary to the suggestion of *Nicolaysen et al* (1953) no tendency to a restitution of the bone tissue lost was observed in the groups of rats maintained on prolonged calcium restriction The continuous loss of bone mineral observed in the present investigation indicates that the old rats failed to adapt to the restricted calcium intake during the experimental period of one year Since the variability in calcium absorption studies is considerable with a reported coefficient of variation of approximately 25 (*Nicolaysen et al* 1953) a slight continuous calcium loss from the skeleton would be difficult to determine with such techniques

With the tetracycline double labelling procedure no difference in the amount of bone surfaces showing new bone formation was observed in the normal control animals and in the osteoporotic rats fed the low calcium diet for 6 to 12 months Neither was any difference in the degree of mineralization noted on microradiographs of undecalcified vertebral bone sections There were further no cellular differences from the normal in decalcified histological sections of bone in the different experimental animals It is concluded therefore that the bone changes induced in the present investigation are in accordance with those of typical osteoporosis as described by *Collins* (1966)

In many earlier animal experiments purporting to demonstrate the effect of calcium deprivation inanition and therefore protein caloric deficiency also occurred (see *Platt et al* 1961 *El Maraghi et al* 1965) This dual aetiology was eliminated in the present experiment in which the animals were kept on a high caloric low calcium diet The possibility of bone atrophy due to inactivity was also excluded

Various morphological changes of the bone tissue i e basophilia of the bone trabeculae fibrosis and increased clasmatocytic activity have been reported to be characteristic of osteoporosis in rats (*McClendon and Blaustein* 1965) However such changes appear to be more typical of osteitis fibrosa than of osteoporosis and were not observed in the present investigation Although areas

by *Jowsey and Raisz* (1968) was apparently transient since in cats fed the low calcium diet for 13 months the osteoid borders, *although highly increased in* frequency were *of normal* width The decrease in resorption but not in formation observed in such animals treated with a high calcium diet for 1 month suggested that the bone changes induced by the low calcium diet could be reversed In adult dogs maintained on a low calcium high phosphorus diet, bone lesions as in osteitis fibrosa have recently been reported (*Saville and Krook* 1968) Histological examination of decalcified bone sections showed the presence of numerous osteoblasts with the appearance of resorption cavities and further osteoblasts and osteoid tissue covering the surfaces of cancellous bone Despite the definitely increased amount of osteoid tissue the calcium accretion rate by bone was *normal* (*Saville and Krook* 1968) This condition suggesting qualitative changes in the bone tissue was called nutritional hyperparathyroidism

Although prolonged deficiency or malabsorption of calcium has been related to the onset of osteoporosis in humans (*Nordin* 1960 1961 1962 1964) and calcium therapy is widely used in the treatment of the condition the relation of calcium deficiency to osteoporosis is not clear (*Dent and Watson* 1966) Of primary importance in this connection is the observation by *Malm* (1958) that a negative calcium balance prevails in human volunteers for a relatively long time after the institution of a low calcium intake In a review of the literature *it has been stated that osteoporosis can be produced in adult animals by a* negative calcium balance usually induced by low calcium diets (*Nordin* 1960) However it was only young growing animals that were studied in these experiments. It is now established that the reaction of the growing skeleton is *quite different to that of the mature skeleton In* young rats the bone lesions correspond to those in typical rickets When there is a rapid reduction in bone mass due to pronounced calcium deficiency osteitis fibrosa or osteomalacia will occur both in growing and in mature animals In the present investigation the development of osteoporosis is described in mature rats placed on a low calcium diet for varying periods *of time from the age of one year Results of* calcium balance studies indicate that the general principle of the adaptation of calcium absorption in old rats can be applied also to other species (*Nicolaysen et al* 1953) The results of the present investigation suggest therefore that prolonged calcium *restriction might contribute* to the onset of symptomatic osteoporosis in adult humans also

In lactating female rats a reduction of the bone tissue has been induced by instituting a low calcium diet (*Tomlin et al* 1953, *McClendon and Blaustein* 1965) These changes were described as osteoporosis and could be reversed by the administration of tricalcium phosphate (*McClendon and Blaustein* 1965) However, the morphological criteria of osteoporosis used suggest that the condition induced was osteitis fibrosa rather than osteoporosis

In 6 month old male rats fed for 20 weeks with a low calcium diet containing 0 26 per cent calcium and 0 45 per cent phosphorus a significant reduction in bone mass and in weight of ash from whole bone was recorded (*Ferguson and Hartles* 1966) Decalcified sections and microradiographs of undecalcified sections from the femur showed no differences from the normal except that the shaft appeared thinner These results are confirmed by those of the present investigation However, as only one observation period was used in the experiment by *Ferguson and Hartles* (1966) no information was obtained concerning the development of the bone reduction Other investigators (*El Maraghi et al* 1965) found little it any effect on the weight of ash/cm³ in the femur in 2 year old rats maintained on a low calcium diet *i e* 0 11 per cent calcium and 0 55 per cent phosphorus for 12 weeks This observation is in agreement with the present results showing that approximately 14 to 16 weeks are required for the development of an evident reduction in bone mass of adult rats fed a similar diet The statement by *El Maraghi et al* (1965) that a dietary calcium concentration of 0 11 per cent would be adequate for maintenance in old rats thus appears to be not valid

Osteoporosis has also been reported in adult cats fed a low calcium high phosphorus meat diet, *i e* calcium 0 007 and phosphorus 0 18 per cent on a wet weight basis (*Jowsey and Gershon Cohen* 1964) After 10 weeks on this diet radiologic evidence of decreased mineral density was found and microradiographs of undecalcified bone sections showed a reduction in the width of bone trabeculae and the appearance of resorption cavities in the cortical bone The increased resorption was accompanied by an increase in number of newly formed osteones Contrary to the experience in clinical osteoporosis the reduction in bone mass was reversed by feeding a high calcium diet In that experiment and in an extended similar study (*Jowsey and Raisz* 1968) the induced bone changes were related to observed secondary hyperparathyroidism Cats fed the low calcium meat diet for 5 months showed definite osteomalacia In the present study no such changes were observed during the development of the osteoporosis The appearance of osteomalacia is probably dependent upon degree of calcium deficiency and the dietary calcium phosphorus ratio The osteomalacia reported

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eosin no osteoclasts were observed either in the normal or in the osteoporotic animals. Sections of *vertebral bone stained with toluidine blue* at pH 4.4 showed in the metaphyseal bone areas with evident metachromasia. No difference in the staining properties of these areas was found between normal and osteoporotic animals.

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SUMMARY

One year old fully grown rats were maintained on a low calcium diet with normal contents of phosphorus and vitamin D for periods varying from 1 week up to 1 year The effect of the treatment upon the skeletal tissue was studied by radiographical microradiographical and histological methods Quantitation of the amount of bone tissue was performed in special bones by the determination of the 'femur score and the vertebral bone 'hits In special whole bones the contents of ash and hydroxyproline and the gross bone density were examined The uptake and distribution of chlortetracycline administered by intraperitoneal injection 10 and 20 days before sacrifice was studied in vertebral bone sections

In the adult rats used the skeletal growth was completed at the start of the experiment By radiologiceal examination performed at the start and at the end of each experimental period, the occurrence of a slight but definite reduction of the cortical thickness of the tubular bones and a decreased density of the trabecular pattern in the metaphyseal bone was found in all animals fed the low calcium diet for 6 months and longer These osteoporotic rats showed significantly lower values for the femur score and the vertebral bone hits than for the normal controls The ash content of the tibia and the hydroxyproline content of the metacarpal bone showed significantly decreasing values during the observation period The six groups of rats kept on a restricted calcium intake for 6 to 12 months showed significantly lower values for the gross bone density of the humerus on comparison with those of the normal controls On microradiographical examination a reduction in the number of vertebral bone trabeculae was observed in the rats fed the low calcium diet for 6 months and longer The remaining bone trabeculae were considerably thinner than normal but no change in degree of mineralization was observed the bone being as evenly mineralized as in the normal rats In these osteoporotic rats the tetracycline fluorescent micrographs had a similar appearance to those in normal rats Thus no apparent difference in the amount of bone surfaces showing fluorescence of newly formed bone was observed On histological examination of decalcified sections stained with haematoxylin

eosin no osteoclasts were observed either in the normal or in the osteoporotic animals Sections of vertebral bone stained with toluidine blue at pH 4 4 showed in the metaphyseal bone areas with evident metachromasia No difference in the staining properties of these areas was found between normal and osteoporotic animals

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Studies on the Development of Experimental Osteoporosis

II The Effect of Prolonged Calcium Restriction on the Blood Calcium Level and the Distribution of Ca^{45} between Blood and Bone in Adult Male Rats

by

Sven Erik Larsson

is longer for old than for young rats (*Henry et al* 1960) According to Nicolaysen et al (1953) a marked adaptation i e a distinctly increased efficiency of calcium absorption will occur in old rats only when they have suffered a substantial loss of calcium from the skeleton in principle this finding agrees with observations in man It has been considered that the increased efficiency of calcium absorption would compensate fully for any previous loss (*Nicolaysen et al* 1953) However in a previous study (*Larsson* 1969 a) the development of a significant reduction in bone mass was found in adult male rats maintained *on a prolonged low calcium intake* for varying periods of up to one year Histological examination revealed that the bone changes induced in these animals *fulfilled the criteria for osteoporosis described by Collins* (1966)

The present investigation was undertaken in order to elucidate the pathomechanisms involved during the development of this type of osteoporosis The study presented here concerns the effect of prolonged calcium restriction in adult male rats on the blood calcium level and the distribution of Ca^{45} between blood and bone after intraperitoneal administration of the isotope

EXPERIMENTAL

The same experimental material was used as in the previous investigation (*Larsson* 1969 a) A total of 95 adult male rats of the Sprague Dawley strain[1] were divided into two experimental series Sixty animals comprised a short term and 35 a long term series Apart from the duration of the test diets both series were treated identically All animals except the controls of the long term series (see below) were stated to be 12 to 12½ months old at the start of the experiment The mean initial body weight of the animals of the two series was 499 0 ± 5 2 and 501 8 ± 9 2 grams respectively The animals had been bred on a standard laboratory ration containing 1 4 per cent Ca and 1 2 per cent P* and adequate amounts of vitamin D

Experimental animals

All the experimental animals were fed the low calcium test diet of General Biochemical Inc Chagrin Falls Ohio The ingredients and composition of this diet have been described in a previous investigation (*Larsson* 1969 a) Chemical

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[1]) Anticimex Co Stockholm

* Here and in the following text the figures based on dry weight are given

INTRODUCTION

In human osteoporosis disturbances in calcium metabolism and the efficiency of calcium homeostasis in maintaining extracellular fluid calcium has been considered to be of major pathophysiological importance for the reduction of bone mass (*Heaney* 1965) in contradistinction to the concept of a primary defect (accelerated ageing of bone) in the bone tissue itself (*Urist* 1962) Studies in osteoporotic patients with bone seeking isotopes have contributed little to our understanding of the osteoporotic process (*Nordin* 1962) Normal skeletal accretion of bone seeking isotopes or stable strontium is generally reported (*Heaney and Whedon* 1958, *Dow and Stanbury* 1960 *Fraser et al* 1960 *Nordin* 1960 *Dymling* 1964) but both reduced accretion (*Bauer et al* 1957, *Eisenberg and Gordan* 1961 *Dymling* 1962 *Bronner et al* 1963 *Lafferty et al* 1964) and increased (*Nordin* 1959) have also been observed However a reduced accretion by the skeleton in osteoporosis may be relative due to reduced bone mass Usually clinical osteoporosis takes several years to develop until the disease can be diagnosed and from results of isotope studies in the osteoporotic patient it is difficult therefore to draw any conclusions concerning the patho mechanisms involved during this prolonged process of bone reduction

Available data obtained from studies with bone seeking isotopes are inconclusive with regard to the skeletal reaction to prolonged calcium restriction in experimental animals A greater retention than normal of a dose of strontium has been reported in calcium deficient young rats (*Harrison and Fraser* 1960) However since the calcium deficient animals failed to grow or to gain weight at the same rate as the control animals it is difficult to interpret the results obtained These findings were not confirmed by *Copp and Suiker* (1962) who observed a reduced retention of Ca^{45} in young rats after dietary calcium restriction In calcium deficient adult rats their data indicated normal Ca^{45} retention and increased bone resorption In calcium deficient pregnant rats the percentage of orally administered Ca^{4} retained has been reported to be 3 5 to 4 0 times that retained by control animals (*Bawden and Osborne* 1962)

The adaptation to a reduced calcium intake has been extensively investigated by balance studies in the rat (*Henry and Kon* 1947 1953 *Barucha and McCay* 1954 *Nicolaysen* 1943 1956 *Henry et al* 1960) Old rats need a minimum of 4 months to adapt themselves to a low calcium intake This period of adaptation

Plasma sampling

Blood was collected from all animals at the time of sacrifice which was performed by bleeding the animal to death from the femoral artery under ether anaesthesia In addition from the animals in the long term series 0 3 to 0 4 ml tail blood was collected at intervals of 12 24 36 and 48 hours following the administration of the iso ope The collected blood was centrifuged immediately at 3 ^v3 r p m for 15 minutes and the supernatant plasma was pipetted into acid washed test tubes and kept at - 20 C pending subsequent analyses

Bone sampling

In the animals of the long term series the right fore paw was removed under light ether anaesthesia 24 hours and the left one 48 hours after the Ca^{45} administration The specimens were then kept at - 20 C for subsequent determination of the Ca^{45} activity of the second metacarpal bone The animals were relatively unaffe ted by the operations After sacrifice both tibiae of the animals of the short term series and the right tibia and the right fifth metatarsal bone of those of the long term serie were taken for isotope studies

Preparation of material for Ca^{45} act ity determinations

A *Whole bone* The following bones were carefully freed of surrounding soft tissues and periosteum a) both tibiae in the animals of the short term series but only the right one in the long term series b) in the animals of the long term series in add tion the right and the left second metacarpal bone and the right fifth metatarsal bone were used

B *Pure cortical bone tissue* In the animals of the long term series the tubular bones ex ept the right tibia and humerus were carefully dissected free from soft tissues and periosteum The ends of the bones and the articular cartilage were removed using a bandsaw The diaphyses were split into small bone fragments wh h were carefully cleaned of all bone marrow no solvents being used The bone fragments were defatted and dehydrated in 5 changes of acetone for 3 days This material was finally air dried and then pulverized using an Intermediate model Wiley Laboratory Mill provided with a 60 mesh sieve The whole bones and approximately 75 mgs of cortical bone powder of all speci mens of ea h series were ashed simultaneously in a muffle furnace at 700 C for 16 hours The exact weight of the ash was determ ned with the aid of a Mettler balan e and with an ac ura y of 0 05 mg The ash of the whole tibia

analyses showed that the diet contained 0 09 per cent Ca and 0 55 per cent P The Ca P ratio was 1 6 1 The diet was supplied with an adequate amount of vitamin D All animals received diet and deionized water *ad libitum* The daily calcium intake was estimated at 18—20 mgs per animal Groups of 5 rats each were kept on this regimen for different periods of time in the short term series ten groups for 1 to 16 weeks in the long term series six groups for 6 to 12 months

Another group of 5 animals was fed the test diet described above supplemented with 4 per cent $CaCO_3$ i e this diet contained a total amount of 1 7 per cent Ca and 0 55 per cent P The Ca P ratio was 1 0 4 This diet and tap water were given *ad libitum* for 16 weeks and the daily calcium intake of these animals was estimated at 340—360 mgs

Control animals

In the short term series one group of 5 rats received a normal laboratory ration[1] containing 1 0 per cent Ca and 0 75 per cent P for 16 weeks The Ca P ratio was 1 0 75 Diet and tap water were given *ad libitum* The daily calcium intake was estimated at 200—220 mgs In the long term series one group of 5 animals was fed the normal laboratory ration and tap water for 4 weeks to accustom the animals to the laboratory routine These animals were stated to be approximately 20 months old when delivered to the laboratory

All the animals were housed five to each cage without access to direct sunlight and at a temperature of 18—20° C The animals moved about freely in the cages No coprophagy was observed The series were planned in such a way that all the animals within each series were sacrificed at the same time In all animals the initial and final body weights were recorded In addition all the animals of the short term series were weighed weekly

Isotope administration

Seventy two hours before sacrifice each animal was injected intraperitoneally with 20 microcuries of Ca^{45} in 1 0 ml physiological saline solution from a single batch of $Ca^{45}Cl_2$ for each series

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1) Ewos Co Sodertalje Sweden

2) Calcium chloride in aqueous solution 2—5 c g Ca C E S 2 The Radio chemical Centre Amersham England

Plasma sampling

Blood was collected from all animals at the time of sacrifice which was performed by bleeding the animal to death from the femoral artery under ether anaesthesia. In addition from the animals in the long term series 0.3 to 0.4 ml tail blood was collected at intervals of 12, 24, 36 and 48 hours following the administration of the isotope. The collected blood was centrifuged immediately at 3 000 r.p.m. for 15 minutes and the supernatant plasma was pipetted into acid washed test tubes and kept at -20 C pending subsequent analyses.

Bone sampling

In the animals of the long term series the right fore paw was removed under light ether anaesthesia 24 hours and the left one 48 hours after the Ca^{45} administration. The specimens were then kept at -20 C for subsequent determination of the Ca^{45} activity of the second metacarpal bone. The animals were relatively unaffected by the operations. After sacrifice both tibiae of the animals of the short term series and the right tibia and the right fifth metatarsal bone of those of the long term serie were taken for isotope studies.

Preparation of material for Ca^{45} activity determinations

A. *Whole bone.* The following bones were carefully freed of surrounding soft tissues and periosteum: a) both tibiae in the animals of the short term series but only the right one in the long term series. b) in the animals of the long term series in addition the right and the left second metacarpal bone and the right fifth metatarsal bone were used.

B. *Pure cortical bone tissue.* In the animals of the long term series the tubular bones except the right tibia and humerus were carefully dissected free from soft tissues and periostrum. The ends of the bones and the articular cartilage were removed using a bandsaw. The diaphyses were split into small bone fragments which were carefully cleaned of all bone marrow, no solvents being used. The bone fragments were defatted and dehydrated in 5 changes of acetone for 3 days. This material was finally air dried and then pulverized using an Intermediate model Wiley Laboratory Mill provided with a 60-mesh sieve. The whole bones and approximately 75 mgs of cortical bone powder of all specimens of each series were ashed simultaneously in a muffle furnace at 700 C for 16 hours. The exact weight of the ash was determined with the aid of a Mettler balance and with an accuracy of 0.05 mg. The ash of the whole tibia

was dissolved in 5 0 ml of 1 2 N hydrochloric acid When the ash was completely dissolved, deionized water was added to the solution to a final volume of 100 ml An aliquot of 2 0 ml was pipetted into a 25 ml polyethylene counting vial which was then filled with a gel scintillator composed of 2 5 Diphenyloxazole (PPO) 1 0 g 1 4 bis 2 (4 Methyl 5 Phenyloxazolyl) Benzene (POPOP) 0 3 g Naphtalane 100 0 g Dioxane 1 litre and thixotropic gel powder (CAB O SIL) to saturation The ash of the small bones and the ash of the cortical bone powder were dissolved directly in 2 0 ml of 1 2 N hydrochloric acid in the counting vials and counting was performed after addition of the scintillator

C *Plasma* The Ca^{45} activity was determined directly using 1 0 ml of plasma collected at sacrifice and about 0 2 ml of plasma obtained from the blood collected from the tail at different intervals after the administration of the isotope This procedure was considered suitable for the purpose of the present study (see *Budy* 1963) and was recommended by *Kumar* (1966) The same scintillator was used as for the bone ash solutions

ANALYTICAL METHODS

Determination of the Ca^{45} activity[1] was carried out in a Packard Tri Carb Liquid Scintillation Spectrometer This counting was performed at + 3°C simultaneously for all the specimens within each series The samples were usually counted 3 x 5 minutes each at least 10 000 impulses being recorded The background was of the magnitude of 25 to 30 c p m The coefficient of variation for the quotient between the two energy channels used was 2 8 to 3 2 per cent The stability of the spectrometer was tested as follows One Ca^{45} sample was counted 60 times during a period of about 15 hours The coefficient of variation was 1 0 per cent *i e* the stability of the apparatus was good Corrections were made for background and decay Corrections for self absorption were not considered necessary because of the constancy of counting efficiency

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[1]) The method for determination of the Ca^{45} activity as used in the Orthop Res labor Presbyterian St Luke s Hosp, Chicago Ill has been applied in this investigation

) Model 314 EX 2 Packard Instruments Co La Grange Ill USA

The calcium content of cortical bone powder was analysed by atomic absorption spectrophotometry with the aid of a Perkin Elmer Model 303 Instrument About 50 mgs of bone powder were ashed as described above The ash was weighed on a Mettler balance and then dissolved in 10 ml of 1 2 N hydrochloric acid After dilution with deionized water to the desired calcium concentration a 5 per cent lanthanum solution in 25 % (v/v) HCl was added so that the final calcium concentration was within an optimum working range of 1 to 10 ppm and with 0 5 per cent lanthanum[1] In this way the calcium lanthanum ratio was 1 1000 as recommended by *Willis* (1961) for suppression of the interference by phosphorus within the solution The added calcium recovery in these bone ash solutions was found to be 98 per cent Duplicate determinations were performed throughout The coefficient of variation for these analyses was less than 1 per cent

The calcium concentration of plasma obtained from the blood collected at sacrifice was determined by flame photometry using an Eppendorf's photometer Duplicate determinations were always performed The error of the method was less than 1 per cent (*Johansson* 1966)

Treatment of isotope data The Ca^{45} activity of bone was expressed as counts per minute per milligram of ash No significant difference was found in the calcium contents of ash from pure cortical bone tissue of the normal and of the calcium deficient animals the mean calcium concentration was 38 09 ± 0 20 per cent Therefore the expression counts per minute per milligram of ash is equivalent to the specific activity and the factor 0 3809 was used when the bone accretion rates were calculated (see below) The Ca^{45} activity of plasma at 72 hours after the isotope injection was expressed as counts per minute per milligram of calcium The plasma Ca^{45} activity curves (Fig 3) were also based upon values expressed as counts per minute per milligram of calcium Because of the necessity of collecting as little blood as possible at the different periods after the Ca^{45} administration plasma calcium determinations were performed only on blood samples obtained at sacrifice

The calcium accretion rates for the whole tibia (mg calcium/hour/mg calcium of the tibia) were calculated according to *Bauer et al* (1955) The mean values within each group were used throughout

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[1]) Perkin Elmer Review May 1966

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[1]) Perkin Elmer Review May 1966

Statistical treatment of data The analytical data obtained from the rats in each group were subjected to analysis of variance with one-way lay out according to *Scheffe* (1961) The hypothesis of no difference between groups was tested at the 5 per cent significance level When a significant result was obtained data for one or more groups were combined in order to find significant contrasts These were tested according to *Scheffe* (1961) The hypothesis of no difference between the data of the group of rats fed the calcium enriched diet and those of the normal control group in the short term series was tested with Student s t test as described by *Brownlee* (1965) A 5 per cent significance level was used In the present study the term significant stands for statistically significant as found with the tests described above

RESULTS

Six deaths occurred among the whole material five among the experimental animals in the long term series and one in the short term series all probably due to advanced age These animals were excluded The remaining animals were in good health The body weights have been reported in a previous study (*Larsson* 1969 a) on the same material

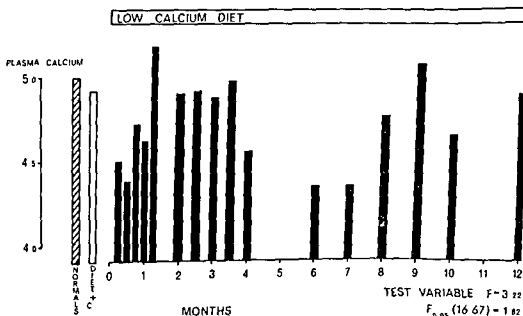


Fig 1 Plasma calcium in rats fed the normal laboratory ration the calcium enriched diet and the low calcium diet

Plasma calcium (Fig 1 Table 1)

The e was no significant difference in plasma calcium between the normal ontrol animals of the short term and the long term series The animals fed the calcium enriched diet for 16 weeks showed sim lar values to those of the control animals In the rats maintained on the low calcium diet for 1 2 3 and 4 weeks subnormal values were noted This fall in plasma calcium was however not significant In the five groups of rats maintained on a low calcium diet for 5 to 14 weeks normal plasma calcium values were observed Subnormal values were again noted in the animals fed the low calcium diet for 4 6 and 7 months Neither was this fall in plasma calcium significant In the four groups

Groups	No of animals	Plasma calcium mEq /l	S E.M	
Normal laboratory ration	10	5 0	0 06	
Low calcium diet for 1 week	4	4 5	0 12	N.S
2 weeks	5	4 4	0 25	
3	5	4 7	0 17	
4	5	4 6	0 20	
5	5	5 2	0 07	
8	5	4 9	0 14	
10 „	5	4 9	0 10	
12	5	4 9	0 23	
14	5	5 0	0 10	
16	5	4 6	0 21	N.S
6 months	4	4 3	0 13	
7	4	4 3	0 12	
8	3	4 8	0 14	
„ 9	5	5 1	0 04	
10 „	5	4 7	0 09	
12 „	4	4 9	0 11	
		$F = 3\ 22$ sign		
		$F_{0\ 9}$ (16 67) = 1 8		
Calcium enriched diet for 16 weeks	5	4 9	0 06	N.S

T ble 1 Plasma calc um n rats fed the normal laboratory ration, the low cal ium d et and the calcium enriched d et

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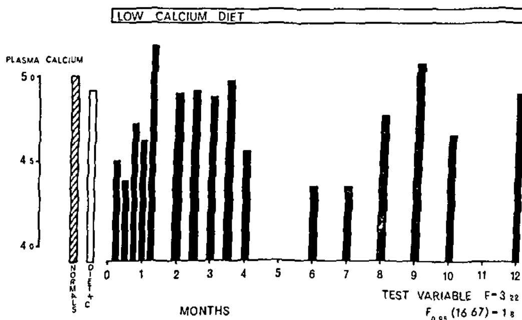


Fig 1 Plasma calcium in rats fed the normal laboratory ration the calcium enriched diet and the low calcium diet

Groups		No of animals	Plasma Ca^{45} CPM/mg calcium	SEM	
Normal laboratory ration		10	21576	1060	
Low calcium diet for	1 week	4	39486	4458	sign
	2 weeks	5	29200	2375	
	3	5	20507	2843	
	4	5	22022	2936	
	5	5	20048	1325	
	8	5	27670	1348	
	10	5	27880	2367	
	12	5	32190	1670	
	14	5	31428	1694	
	16	5	36705	3932	
	6 months	3	96054	4947	sign
	7	4	65638	2471	
	8	3	63640	10454	
	9	4	62257	8623	
	10	3	51886	7233	
	12	3	87780	6714	
			F = 35 27 sign		
			$F_{0\ 5}$ (16 62) = 1 82		
Calcium enriched diet for 16 weeks		5	12224	631	sign

Table 2 Plasma Ca specific activity 72 hours after the intraperitoneal injection of 20 microcuries of Ca [5] per animal in rats fed the normal laboratory ration the low calcium d et and the calcium enriched diet

1 week showed significantly increased values compared with those of the rats fed the normal laboratory ration The animals fed the low calcium diet for 3 to 5 weeks showed approximately the same values as those of the normal controls Significantly higher values were noted in animals maintained on a restricted calcium intake for 8 weeks to 1 year This difference was most pronounced in the groups treated for 6 to 12 months The rats fed the calcium enriched diet for 16 weeks showed significantly lower values compared with those of the normal controls

of animals maintained on the low calcium diet for 8 to 12 months the plasma calcium showed no significant change The reductions in plasma calcium amounted to approximately 12 per cent in the groups of rats kept on the low calcium diet for 2 weeks and 6 and 7 months

The plasma Ca^{45} specific activity at 72 hours after the Ca^{45} injection (Fig 2 Table 2)

The values of the two control groups fed the normal laboratory ration showed no significant difference The group of rats kept on a low calcium intake for

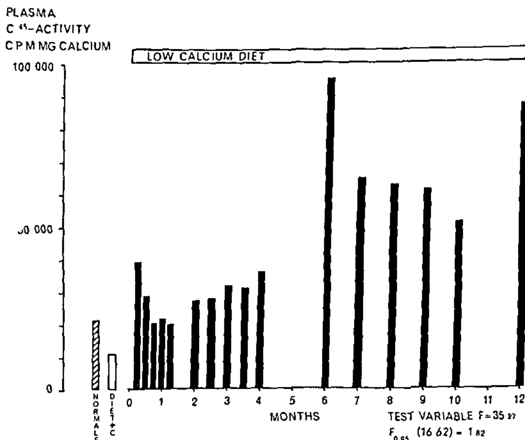


Fig 2 Ca^{45} activity in plasma 72 hours after the intraperitoneal administration of 20 microcuries of Ca^{45} per animal in rats fed the normal laboratory ration the calcium enriched diet and the low calcium diet

Groups	No of animals	24 hours after Ca^{45} inj CPM/mg ash M C II dx	SEM	48 hours after Ca^{45} inj CPM/mg ash M C II sin	SEM	72 hours after Ca^{45} inj CPM/mg ash M T V dx	SEM
Normal laboratory ration	5	117 5	5 9	107 0	7 1	99 4	2 7
Low calcium diet for 6 months	3	162 5	13 8	162 6	8 5	177 9	16 2
7	4	132 8	5 1	118 2	5 7	148 9	8 6
8	3	136 0	8 9	128 4	5 3	148 0	9 0
9	5	132 9	6 1	136 6	11 2	142 2	8 4
10	4	137 7	4 4	132 7	9 6	152 3	8 4
12	3	130 5	9 7	130 9	3 4	153 5	6 6
		F = 3 13 sign		F = 3 89 sign		F = 8 33 sign	
				$F_{0.05}$ (6 20) = 2 60			

Table 3 Bone Ca^{45} activity at different times after the intraperitoneal injection of 20 microcuries of Ca^{45} per animal in rats fed the normal laboratory ration and the low calcium diet (M C II dx = right 2nd metacarpal bone M C II sin = left 2nd metacarpal bone M T V dx = right 5th metatarsal bone)

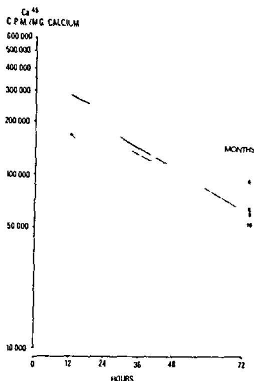


Fig 3 Ca^{45} specific activity in plasma 12 24 36 48 and 72 hours after the isotope administration in rats fed the normal laboratory ration (broken line) and rats fed the low calcium diet for 6 to 12 months (uninterrupted lines) Each point is the mean value of the control group Logarithmic graph

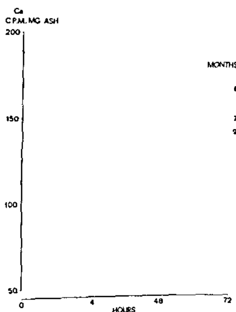


Fig 4 Ca^{45} activity of small bones 24 48 and 72 hours after the isotope administration in rats fed the normal laboratory ration (broken line) and rats fed the low calcium diet for 6 to 12 months (uninterrupted lines)

values were significantly higher at all periods after the Ca^{45} injection in all the experimental groups and showed a slight increase with time after the isotope injection In contrast the values obtained from the rats of the control group showed a slight decrease progressing with time after the injection of the isotope

The Ca^{45} activity of the tibia 72 hours after the Ca^{45} injection (Fig 5 Table 4)

The values of the two groups of rats fed the normal laboratory ration showed no significant difference

In the rats fed the low calcium diet for 1 to 4 weeks successively higher values were found compared with those of the normal controls with a maximum increase by approximately 100 per cent in the 3rd and 4th weeks In the

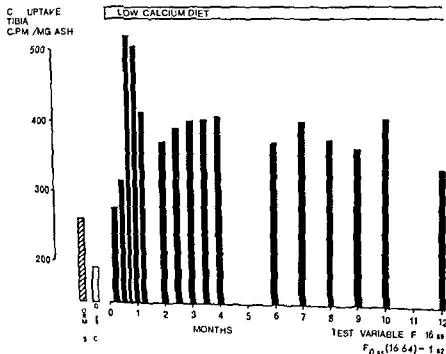


Fig 5 The uptake of Ca in the tibia *72 hours after* the intraperitoneal administration of 2 microcuries of Ca^{45} *in rats fed the normal laboratory* ration the calcium enriched diet and the low calcium diet

The plasma Ca^{45} activity at different periods after the Ca^{45} injection was examined in the long term series (Fig 3) All groups maintained on prolonged calcium restriction showed consistently higher values than those of the control group The Ca^{45} activity showed throughout a decrease with time after the injection, which was more rapid for the control group than for the experimental groups

The Ca^{45} activity of small bones at different periods after the Ca^{45} injection was also examined in the long term series (Fig 4 Table 3) In all experimental groups consistently higher values were obtained than in the control group The

Groups		No of animals	Ca^{45} activity C P M /mg ash	S E M	
Normal laboratory ration		9	260 9	5 8	
Low calcium diet for	1 week	4	276 0	16 4	
	2 weeks	5	317 1	18 7	
	3	5	520 7	5 7	sign
	4	5	504 5	21 3	
	5	5	412 9	15 4	
	8	5	369 7	15 0	
	10	5	388 4	10 1	
	12	5	400 9	15 4	
	14	5	402 7	13 3	
	16	5	406 3	11 9	
	6 months	4	370 5	41 6	
	7	4	401 1	20 5	
	8	3	375 0	18 2	
	9	5	371 8	18 9	
	10	4	405 0	31 5	
	12	3	334 1	16 2	
			F – 16 89 sign		
			$F_{0\ 05}$ (16 64) = 1 82		
Calcium enriched diet for 16 weeks		4	188 6	20 0	sign

Table 4 The Ca^{45} uptake of the tibia (c p m /mg ash) 72 hours after the intraperitoneal injection of 20 microcuries of Ca^{45} per animal in rats fed the normal laboratory ration the low calcium diet and the calcium enriched diet

The calcium accretion rate for the tibia (*Table 6*)

The accretion rate (mg calcium/hour/mg calcium of the tibia) was examined in the rats of the long term series. In the group of rats fed the low calcium diet for 6 months the mean accretion rate was lower than in the control group. *The four groups of animals maintained on a low calcium intake for 7 to 10 months showed approximately the same mean values as for the control group.* Finally a lower accretion rate was found in the group of rats kept on a restricted calcium intake for 12 months compared with that in the control group.

Groups		ACCRETION RATE (mg Ca/hour/mg Ca of the tibia)
Normal laboratory ration		11.34 × 10–[illegible]
Low calcium diet for	6 months	6.57 × 10–[illegible]
	7	10.89 × 10–[illegible]
	8	10.30 × 10–[illegible]
	9	10.09 × 10–[illegible]
	10	10.50 × 10–[illegible]
	12	7.69 × 10–[illegible]

Table 6. The mean calcium accretion rate for the tibia in rats fed the normal laboratory ration and the low calcium diet.

DISCUSSION

Material from the same animals was studied in a previous investigation and it was then found that there was *no significant difference in femur length* between normal and experimental animals and that the skeletal growth and calcification were completed in these rats. The degree of mineralization studied by microradiography of undecalcified sections of vertebral bone was the same in normal and osteoporotic animals (*Larsson* 1969 a).

following 5 to 6 week groups the Ca^{45} uptake was increased by approximately 60 per cent The increased Ca^{45} uptake observed between the 3rd and the 16th week of treatment was statistically significant The six groups of rats kept on a restricted calcium intake for 6 to 12 months showed a consistently increased isotope uptake by the tibia by approximately 40 per cent of that of the control group When the combined values of all these groups were compared with the control group the increase was found to be significant The animals fed th calcium enriched diet for 16 weeks showed a significantly decreased Ca^{45} uptake compared with that of the control animals

The Ca^{45} activity of cortical bone 72 hours after the Ca^{45} injection (Table 5)

The Ca^{4} uptake was further examined in cortical bone powder obtained from the rats of the long term series In the rats maintained on the low calcium diet for 6 to 9 months the values obtained were approximately 20 per cent higher than in the normal control group The two groups of animals fed the low calcium diet for 10 and 12 months showed only slightly higher values than those of the control group

Groups		No of animals	Ca^{4} activity C P M /mg ash	S E M
Normal laboratory ration		5	64 6	2 7
Low calcium diet for	6 months	4	86 7	7 7
	7	4	86 3	3 6
	8	3	73 9	2 5
	9	5	74 0	3 0
	10	4	65 8	4 6
	12	3	69 7	5 6
			F = 4 23 sign	
			$F_{0\ 1}$ (6 21) = 2 58	

Table 5 The Ca^{4} uptake of compact bone powder (c p m /mg ash) 72 hours after the intraperitoneal injection of 20 microcuries of Ca^{4} per animal in rats fed the normal laboratory ration and the low calcium diet

(*Copp et al* 1960) is exquisitely well regulated by means of a negative feedback (*McLean and Urist* 1955) Normally the strain of rats used in the present study shows a markedly constant blood calcium During an 8 week period 8 adult normal male rats showed a *blood calcium concentration of 4 8 – 4 9 mEq/l* and the standard error of the mean with the same analytical method used in the present investigation ranged from 0 02 – 0 06 (*Johansson 1966*) *Eventual seasonal* variations as reported by *Biering* (1950) were eliminated in the present study since all blood samples were collected and analyses were performed on all animals within each experimental series at the same time Neither was there any *significant difference in the* blood calcium level of the control groups of each series *In* short term infusion *experiments on dogs* an attempt was made to evaluate quantitatively the effectiveness of negative feedback in regulating *blood* calcium. The findings in those experiments support the view that the constancy of blood calcium is not due to an extremely efficient homeostatic regulation but must result in part from the relatively small stresses positive or negative calcium loads which are normally placed upon the system (*Hausmann and Riggs* 1966) *The recurrent decreases in the* blood *calcium level observed at different periods of time in the present investigation and which were followed by normalization* were probably due to the large stresses induced by the prolonged calcium restriction upon the mechanisms involved in blood calcium regulation

Low calcium diets with a high phosphorus content have been reported to result in a fall of the blood calcium in different species *e g* adult dogs (*Saville and Krook* 1968) adult cats (*Jowsey and Raisz* 1968) and adult rats (*Engfeldt et al* 1954) In the present investigation it was found that the restriction of calcium *alone with an adequate supply of phosphorus and vitamin D also causes a reduction of the b*lood calcium level It is well known that there is a relationship between dietary levels of calcium and phosphorus and the parathyroids and further between high blood phosphorus concentration and depressed blood calcium although the exact mechanism of these effects is not clear (*Nordin* 1961) However decreased blood calcium has been reported in different species after institution of low calcium diets with *very varying* Ca P ratios such as *e g* 1 45 (*Jowsey and Raisz* 1968) 1 16 (*Engfeldt et al* 1954) 1 10 (*Saville and Krook* 1968) 1 6 1 (*the present investigation*) and 1 15 (*Campbell and Douglas* 1965) With regard to the relation between reduced calcium intake and the development of osteoporosis in humans *it is of interest* that a slight fall in the blood calcium level occurs at different periods of time in adult rats during prolonged calcium restriction when the *diet is normal in* phosphorus and vitamin D It is likely that this also occurs when the low

Although there is usually no abnormality in blood biochemistry in clinical osteoporosis disturbances in calcium metabolism and the efficiency of calcium homeostasis in maintaining extracellular fluid calcium have been considered as the primary pathomechanism for the development of osteoporosis in humans (*Heaney* 1965) In this respect, it was considered of great interest to follow the changes in the blood calcium level and the distribution of Ca^{45} between blood and bone during the development of osteoporosis induced in these adult rats by prolonged calcium restriction It has been reported earlier that old rats need a minimum of 0 5 per cent calcium in the diet for equilibrium (*Henry and Kon* 1947) By feeding a diet containing 0 13 per cent calcium and 0 38 per cent phosphorus old rats remain in negative calcium balance for at least 4 months (*Henry et al* 1960) In the present study adult male rats were maintained on a similar low calcium diet containing 0 09 per cent calcium and 0 55 per cent phosphorus with adequate amounts of vitamin D for periods varying from 1 week up to 12 months Because of this restriction of the calcium intake the animals treated for 14 to 16 weeks and longer developed significant skeletal changes characteristic of osteoporosis (*Larsson* 1969 a)

It was found in the present study that during the development of osteoporosis slightly subnormal blood calcium values appeared not only initially but also at later periods of time with normalized values meanwhile Corresponding to the transient initial fall in blood calcium induced in the present investigation by changing from a normal to a low calcium intake subnormal blood calcium has been reported in healthy humans also after instituting a low calcium diet (*Nordin* 1964 *MacFadyen et al* 1965, *Nordin et al* 1965) This fall of the blood calcium level is certainly due to the large stresses upon the mechanisms involved in blood calcium regulation during a period of negative calcium balance The hypocalcemia of calcium deprivation in humans is believed to be transient and very small changes in blood calcium concentration are considered to be corrected by bone mineral without the intervention of the parathyroid glands due to the existence of a genuine steady state between bone mineral and tissue fluid (*Nordin et al* 1965) However the results of the present study indicate that subnormal blood calcium values occur at different periods of time during prolonged calcium restriction and that these changes are relatively slowly corrected by bone mineral (see below) The falls in the blood calcium level recorded in the present investigation were further of such a magnitude that stimulated parathyroid activity might have been involved for the normalization of the blood calcium concentration

Under normal circumstances the well documented constancy of blood calcium

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After this initial phase there was a further rapid change in the distribution of Ca^{45} Despite a continued subnormal blood calcium concentration there was a decrease to the normal level of the specific activity of Ca^{45} in the blood during the 3rd week of maintained calcium restriction At the same time there was a shift to a corresponding increase by approximately 100 per cent in the deposition of Ca^{45} into bone mineral The same distribution of Ca^{45} was observed during the 4th and 5th weeks of calcium restriction These findings indicate indirectly that the subsequent normalization of blood calcium after the hypocalcemic period was brought about by increased bone resorption and mobilization of skeletal calcium to the blood The observed increase in the deposition of Ca^{45} into bone mineral appears to be secondary to the still more augmented mobilization of bone calcium

During the 5th week of calcium deficiency the blood calcium returned to normal and subsequently remained at a normal level until the 14th week Initially in this period there was another shift in the distribution of Ca^{45} between blood and bone Thus at the 8th week of calcium restriction the Ca^{45} activity of both blood and bone had reached a level 50 to 60 per cent above that of the normal controls Thereafter this distribution of Ca^{45} remained unchanged until the 16th week

These results clearly demonstrate a continued increased level of calcium retention during negative calcium balance induced by the maintained calcium restriction In contrast the group of rats fed the test diet enriched with calcium showed significantly decreased Ca^{45} activity in both blood and bone in comparison with the normal controls The fact that all animals received the same dose of Ca^{45} regardless of their body weight does influence the present results but only to quite a small extent The higher final body weight of the experimental animals compared with the controls was due to an increase in adipose tissues in the former With such an increase in adipose tissues the percentage total body water is reduced (Ljunggren et al 1957) This would imply that the experimental animals would have been afforded more Ca^{45} compared with that of the normal controls if the administered dose had been related to body weight The results of the present study confirm earlier observations that animals accustomed to a high calcium intake must adjust their absorptive mechanism to a lower supply of calcium (Carlsson 1951 Hansard et al 1951 Nicolaysen et al 1953 Henry et al 1960) It must be pointed out that this situation is quite different from that when the intake of calcium is low throughout life In these circumstances rats bred on a low calcium diet remain in calcium equilibrium at levels which would lead to negative calcium balance in rats

calcium intake is combined with various levels of dietary phosphorus Changes in calcium metabolism and in the mechanisms involved in calcium homeostasis might then be expected in prolonged calcium restriction in aged humans also

The described changes in the blood calcium level and the distribution of Ca^{45} between blood and bone 72 hours after the intraperitoneal administration of the isotope (Fig 6) provide special interest, especially with regard to the development of osteoporosis Thus the normal distribution of Ca^{45} rapidly changed upon restriction of the calcium intake After only 1 week of calcium deficiency the rats showed an increase by approximately 100 per cent in the Ca^{45} specific activity in the blood and a slightly increased Ca^{45} activity in bone indicating increased calcium retention This was probably the result of decreased endogenous Ca^{45} and to a minor degree decreased urinary Ca^{45} secondary to the observed fall in blood calcium The adaptation of the rat to a reduced calcium intake is brought about by increased absorption of calcium and results in a decrease of the endogenous calcium (*Nicolaysen et al* 1953 *Henry et al* 1960) Also in humans adaptation to a reduced calcium intake is effected by a more efficient absorption (*Malm* 1958 *Thorangkul et al* 1959)

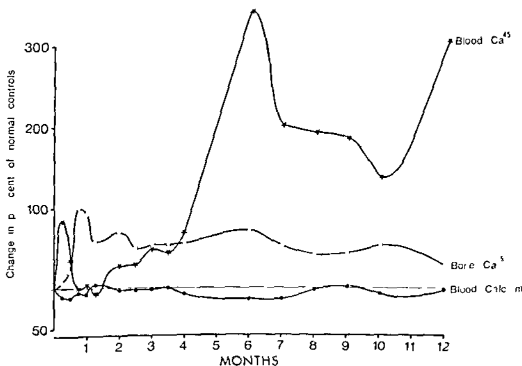


Fig 6 For explanation see text above

in trabecular compared with cortical bone tissue As for the whole tibia the Ca^{45} activity of the cortical bone powder in the present study was significantly higher for the long term calcium deficient rats than for the normal controls In the 6 groups of rats fed the low calcium diet for 6 to 12 months the mean Ca^{45} uptake by the cortical bone was only 19 per cent higher while the mean uptake by the whole tibia was 41 per cent higher than in the normal controls Contributory factors to these differences of 19 to 41 per cent might be the structural changes in cancellous bone described above and further the higher Ca^{45} activity of the bone marrow blood in the osteoporotic animals compared with the normal controls

The Ca^{45} uptake by the small bones at different time intervals after the administration of the isotope showed a significant increase progressing with time after the isotope injection in the groups of rats maintained on prolonged calcium restriction while there was a slight tendency to a decrease in the normal control group This difference could be explained by the consistent high Ca^{45} activity in the blood in the calcium deficient groups which would afford the bone more Ca^{45} to be built in compared with the normal controls

In clinical osteoporosis the bone accretion rate or mineralization rate is usually reported to be normal (*Heaney and Whedon* 1958 *Fraser et al* 1960 *Dow and Stanbury* 1960 *Dymling* 1964 *Nordin et al* 1964) although both reduced accretion (*Bauer et al* 1957 *Eisenberg and Gordan* 1961 *Dymling* 1962 *Bronner et al* 1963 *Lafferty et al* 1964) and increased accretion (*Nordin* 1959) have also been observed *It was therefore considered of interest to estimate the calcium accretion rate in the osteoporotic animals of the present study* Estimations were performed on the whole tibia (mg calcium/hour/mg calcium of the tibia) of the rats of the long term series In the group of rats maintained on a low calcium diet for 6 months a lower mean accretion rate was found than in the control group whereas in the groups kept on a restricted calcium intake for 7 8 9 and 10 months approximately the same values were found as in the normal control group Finally the group of animals fed the low calcium diet for 12 months also showed a decreased accretion rate In 4 month old rats fed a low calcium diet (calcium 0 037 per cent, phosphorus 0 45 per cent) for 6 months a normal accretion rate was found while the resorption was increased (*Copp and Suiker* 1962) These results are in agreement with those of the present study However in the study of *Copp and Suiker* (1962) the effect of the treatment upon the skeletal tissue was not investigated further The findings concerning the rate of calcium accretion in the present investigation indicate that the skeleton rendered osteoporotic by prolonged

bred on a higher or normal calcium diet (*Henry and Kon* 1953, *Nicolaysen* 1956) A similar adaptation is also well documented for humans (for ref see *Henry and Kon* 1953 *Malm* 1958)

With the continuation of the restricted calcium intake a slightly subnormal blood calcium was again observed in the rats kept on the low calcium diet for 16 weeks and 6 and 7 months At the 8th month of calcium restriction a normalization of the blood calcium concentration occurred and thereafter it remained normal until the 12th month A shift in the Ca^{45} distribution indicated that a new dynamic balance was induced in these animals by the prolonged calcium deficiency Thus, the Ca^{45} specific activity in blood showed an increase by 100 to 200 per cent while the Ca^{45} activity in bone was increased by only about 40 per cent In these animals the contribution of structural changes in cancellous bone to the balance and distribution of calcium must be considered With the development of osteoporosis there is a loss of cancellous bone and of cortical bone from the endosteal surfaces as described in the first part of the present investigation (*Larsson* 1969 a) The amount of bone surfaces available for intensive calcium deposition i e surface accretion is reduced There was, further, no apparent change in the amount of bone surfaces showing new bone formation as observed with the tetracycline double labelling technique This demonstrates the importance of always considering these circumstances in dynamic calcium studies of normal and osteoporotic individuals Except for a change in the distribution of Ca^{45} between blood and bone due to the observed reduction of cancellous bone an accelerated calcium absorption i e a further decrease in endogenous Ca^{45}, as suggested by *Nicolaysen et al* (1953) and *Henry et al* (1960) would also contribute to the highly elevated Ca^{45} specific activity in blood observed in the osteoporotic rats By this regulation of the calcium distribution and by increased mobilization of bone calcium the blood calcium concentration can be sustained in prolonged negative calcium balance

The sequence of events reported here demonstrates that in induced negative calcium balance the efficiency of calcium homeostasis in maintaining extracellular fluid calcium is the primary pathomechanism for the development of calcium deficiency osteoporosis

The Ca^{45} activity of pooled cortical bone powder 72 hours after administration of the isotope was found to be less than 1/4 of that of the whole tibia in the normal animals This relationship is of about the same order of magnitude as the corresponding ratio of tibia shaft to whole tibia found in normal young rats by *Bauer and Carlsson* (1955) It is well established that the calcium metabolism is more intensive in the ends than in the shaft of long bones and

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calcium restriction retains calcium to approximately the same extent as the normal skeleton, although a reduced accretion was found in some groups of rats These results are in good agreement with those generally reported for human osteoporosis However when the rate of calcium accretion by bone in osteoporotic individuals is compared with that in normals, differences in bone mass must be considered Furthermore the higher Ca^{45} activity in the bone marrow blood of the osteoporotic animals in the present study compared with that of the normal controls will also influence the obtained values It must be pointed out moreover that bone accretion cannot be equated with bone formation which has been done in many earlier studies In the present investigation calcium accretion is interpreted as a measure only of the retention of calcium by the whole bone and not of the formation of new bone In a previous study (*Larsson* 1969 a), no appreciable difference from the normal was found in the amount of bone surfaces showing new bone formation as estimated by the tetracycline labelling method Normal female rats of the same strain and age as the normal male rats of the present study showed a lower frequency of tetracycline labelled surfaces of the vertebral bone (*Larsson* 1969 b) and also a lower bone Ca^{45} retention (*Larsson* 1969 c) These findings might indicate some relationship between accretion and bone formation Nevertheless it is well known that the amount of tracer localized as diffuse uptake in the bone tissue is both high and variable and this usually makes such a correlation difficult to establish (*Rowland* 1960)

In the pathogenesis of generalized osteoporosis in humans a low intake or malabsorption of calcium has been considered to play an important role (*Nordin* 1960 1961 1962 1964) as well as the efficiency of calcium homeostasis (*Heaney* 1965) After the institution of a low calcium diet in human volunteers a negative calcium balance has been observed for relatively long periods of time (*Malm* 1958) However there is no evidence to prove that calcium deficiency really gives rise to osteoporosis in humans The adaptation to a low calcium intake has been studied extensively in old rats by calcium balance techniques (*Henry and Kon* 1947 1953 *Baruchs and McCay* 1954 *Nicolaysen* 1943 1955 *Henry et al* 1960) In humans principally the same adaptory mechanisms are responsible as in the rat (*Nicolaysen et al* 1953) In a previous investigation (*Larsson* 1969 a) the development of osteoporosis was observed in old rats after prolonged calcium restriction The findings presented here show that significant changes in the calcium dynamics occur during this process of bone reduction It is suggested that this course of events proceeds in different phases in the adaptation to a low calcium intake Initially and also later the

blood calcium level is subnormal due to the low calcium intake Because of the efficiency of calcium homeostasis the blood calcium level is normalized The Ca^{45} data presented here indicate indirectly that this normalization of the blood calcium level is brought about by increased bone resorption mobilizing skeletal calcium to the blood at the expense of the bone mass

SUMMARY

One year old fully grown rats were maintained on a low calcium diet with normal contents of phosphorus and vitamin D for periods varying from 1 week up to 1 year Seventy two hours before sacrifice 20 microcuries of Ca^{45} were administered to each animal by intraperitoneal injection and the Ca^{45} activity in plasma and bone was compared with that of normal controls and in addition with that of animals fed the test diet enriched with calcium

The plasma Ca^{45} activity 72 hours after the isotope injection showed increased values by 100 per cent in the group of rats fed the low calcium diet for 1 week when compared with that of the normal controls The groups of animals kept on a restricted calcium intake for 3 and 4 weeks showed the same values as the controls In these experimental groups there was a significant increase by 100 per cent in the deposition of Ca^{45} into the skeleton while there was a concomitant slight fall in the plasma calcium In the groups of rats fed the low calcium diet for 8 to 14 weeks the plasma calcium was normal and in these groups there was an increase in the plasma and bone Ca^{45} activity by 50 to 60 per cent In the groups of animals kept on the low calcium intake for 4 to 7 months the plasma calcium was again slightly reduced These groups and those treated for 9 to 12 months showed an increase in the plasma Ca^{45} activity by 100 to 200 per cent whereas the Ca^{45} activity in bone was increased by 40 per cent The groups treated for 8 to 12 months showed normalized plasma calcium In the group of rats fed the diet enriched with calcium the plasma Ca^{45} activity was 40 per cent lower and the bone Ca^{45} activity 60 per cent lower than in the control group The plasma calcium showed normal values

The calculated calcium accretion rate for the tibia (mg calcium/hour/mg calcium of the tibia) was described in rats fed the low calcium diet for 6 and

calcium restriction retains calcium to approximately the same extent as the normal skeleton although a reduced accretion was found in some groups of rats These results are in good agreement with those generally reported for human osteoporosis However, when the rate of calcium accretion by bone in osteoporotic individuals is compared with that in normals differences in bone mass must be considered Furthermore the higher Ca^{4} activity in the bone marrow blood of the osteoporotic animals in the present study compared with that of the normal controls will also influence the obtained values It must be pointed out moreover that bone accretion cannot be equated with bone formation which has been done in many earlier studies In the present investigation calcium accretion is interpreted as a measure only of the retention of calcium by the whole bone and not of the formation of new bone In a previous study (*Larsson* 1969 a) no appreciable difference from the normal was found in the amount of bone surfaces showing new bone formation as estimated by the tetracycline labelling method Normal female rats of the same strain and age as the normal male rats of the present study showed a lower frequency of tetracycline labelled surfaces of the vertebral bone (*Larsson* 1969 b) and also a lower bone Ca^{45} retention (*Larsson* 1969 c) These findings might indicate some relationship between accretion and bone formation Nevertheless it is well known that the amount of tracer localized as diffuse uptake in the bone tissue is both high and variable and this usually makes such a correlation difficult to establish (*Rowland* 1960)

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The calculated calcium accretion rate for the tibia (mg calcium/hour/mg calcium of the tibia) was described in rats fed the low calcium diet for 6 and

12 months, while in rats treated for 7 8 9 and 10 months the values were approximately the same as in the control group

The results show that a slight initial fall in plasma calcium occurs on instituting a low calcium diet to adult rats, and also at later stages subnormal plasma calcium values can be observed The findings concerning Ca^{45} indicate indirectly that the normalization of plasma calcium is brought about by increased mobilization of skeletal calcium to the blood This results in a reduction of bone mass and the development of o teoporosis

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12 months, while in rats treated for 7, 8 9 and 10 months the values were approximately the same as in the control group

The results show that a slight initial fall in plasma calcium occurs on instituting a low calcium diet to adult rats, and also at later stages subnormal plasma calcium values can be observed The findings concerning Ca^{45} indicate indirectly that the normalization of plasma calcium is brought about by increased mobilization of skeletal calcium to the blood This results in a reduction of bone mass and the development of osteoporosis

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Studies on the Development of Experimental Osteoporosis

III The Effect of Combined Oophorectomy and Prolonged Prednisolone Administration on the Skeletal Tissue of Adult Rats

by

Sven Erik Lars on

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treatment results after 100 days in radiographically evident *osteoporosis* Oestradiol cures the osteoporosis in these animals despite continuous cortisone administration while only very slight *improvement* occurs in rats given testosterone (*Caldwell* 1962) The curative effect of oestrogens has also been observed in birds rendered severely osteoporotic with large doses of ACTH or cortisone (*Urist* 1958) In young rats but *not in other* animals oestrogens inhibit bone resorption (*Budy et al* 1952 *Lindquist et al* 1960)

The inhibitory effect of excess cortisone upon normal skeletal growth is well known In the experiments performed on rabbits young growing animals *were* used and in addition to the osteoporotic changes inhibited bone growth was observed (*Sissons and Hadfield* 1955 *Storey* 1957 *deValderrama and Munuera* 1965) This inhibitory effect is also well documented *for young rats* (*Follis* 1951 *Laron et al* 1958 *Kowalewski* 1962 *Stanisavljevic et al* 1962 *Hulth and Olerud* 1963 *Tapp* 1966) As far as the young growing animal is concerned both interference with normal skeletal growth and a possible eventual effect on the calcium metabolism must be taken into consideration In view of the inhibitory effect of cortisone on the formation of connective tissues (*Asboe Hansen* 1961) inhibited synthesis of bone matrix *is furthermore to be expected*

The present investigation was undertaken in order to examine the effect of combined oophorectomy and prednisolone administration on the mature skeleton of *one year old* fully grown rats and to study the eventual development of skeletal changes during the progress of treatment The aim of this study was to determine whether this hormonal disturbance does in fact give rise to bone reduction *of the mature skeleton of* the adult rat as might be expected from the results concerning growing rats in the experiments of *Caldwell* (1962)

EXPERIMENTAL

Animals

A total of 55 adult female rats of the Sprague Dawley strain[1] were used All animals were stated to be 11 ± to 12 months old at the start of the experiment and their mean initial body weight was 348 5 ± 2 7 grams The animals were divided at random into ten experimental groups and one control group of 5

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[1] Anticimex Co Stockholm Sweden

INTRODUCTION

The hypothesis that oestrogen deficiency is the cause of human osteoporosis was advanced by *Albright and Reifenstein* (1948). This hypothesis was modified to include the possibility that senile as well as other forms of osteoporosis are caused by a state of lack of balance between anabolic or gonadal hormones and anti-anabolic or adrenal corticoid hormones (*Reifenstein* 1957). Hypercorticoidism of endogenous origin in humans is often associated with osteoporosis (*Follis* 1951). Osteoporosis is moreover one of the most serious complications in prolonged cortisone therapy (*Bunim et al.* 1955, *Rosenberg* 1958).

Osteoporosis has been induced experimentally in young rabbits by cortisone administration (*Sissons and Hadfield* 1955, *Storey* 1957). *Sissons* (1956) pointed out the similarity of these lesions to those observed in Cushing's disease. As far as the rabbit is concerned, it has been concluded that the effect of cortisone is inhibitory to new bone formation and that bone rarefaction is due to the unopposed continuance of the normal osteolytic processes (*Sissons and Hadfield* 1955, *Sissons* 1956). From histological observations it has also been deduced that cortisone osteoporosis results not only from a cessation of bone formation but primarily from a direct degrading effect which causes a massive resorption of bone (*deValderrama and Munuera* 1965).

Unlike the rabbit, the young growing rat does not always develop osteoporosis after cortisone administration. Instead, dense metaphyseal bone has been observed. This was believed to be due to delayed bone resorption (*Follis* 1951). However, when the dietary Ca and P are lowered or the ratio altered during cortisone administration, also young rats develop osteoporosis similar to that seen in rabbits treated with cortisone. In cortisone treated rats maintained on a diet containing 1.5 per cent Ca and 1.0 per cent P, increased density of the metaphyseal bone occurs. At a normal Ca:P level, *i.e.* 1.0 per cent Ca and 0.6 per cent P, or a reduced level, osteoporosis develops. This difference in the reaction of the bone has been believed to be associated with the well developed adaptive calcium metabolism of young rats (*Storey* 1960).

Growing male rats subjected to bilateral adrenalectomy and orchidectomy become more sensitive to cortisone. In spite of a high calcium intake, cortisone

treatment results after 100 days in radiographically evident osteoporosis Oestradiol cures the *osteoporosis in these animals* despite continuous cortisone administration while only very slight improvement occurs in rats given testosterone (*Caldwell* 1962) The curative effect of oestrogens has also been observed in birds rendered severely osteoporotic with large doses of ACTH or cortisone (*Urist* 1958) In young rats but not in other animals oestrogens inhibit bone resorption (*Budy et al* 1952 *Lindquist et al* 1960)

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rats each The experimental animals were oophorectomized under ether anaesthesia via a midline abdominal incision under sterile conditions The identification of the first ovaries removed was verified by histological examination All the animals recovered very quickly after the operation No postoperative complications were observed From the third day after oophorectomy each animal received 2 5 mg prednisolone[1] daily dissolved in their drinking water which was supplied intermittently in such a way that the prednisolone was consumed within 1—2 hours The periods of prednisolone treatment varied from 1 to 16 weeks The *control* group consisted of *normal* rats and was observed for 16 weeks These animals were not oophorectomized and received no prednisolone but were otherwise treated in the same way as the experimental animals

The animals were housed individually in screen bottomed wire cages in a separate room without access to direct sunlight and with a room temperature of 18—20°C All animals received the same laboratory ration and tap water in unrestricted quantities except for the intermittent supply of drinking water in the experimental animals during administration of prednisolone, as mentioned above Chemical analysis of the diet given showed that it contained a total of 1 0 per cent calcium and 0 55 per cent phosphorus The quantity of food consumed was estimated for one animal of each group during a period of 5 days starting at the 7th day before sacrifice by recording daily the weight of the pellets given to each animal and the weight of the food not consumed No antibiotics were given The series were planned so that all the animals were sacrificed at the same time This was performed by bleeding them to death from the femoral artery under ether anaesthesia

Methods

The methods used are essentially the same as described in greater detail in a previous paper (*Larsson* 1969 a)

Body weight and weight of the adrenals

All the animals were weighed weekly From all animals the adrenal glands were removed after sacrifice The glands were dissected free from all surrounding fat tissue they were immediately placed in weighing containers and their wet weight was recorded on a Mettler balance with an accuracy of 0 05 mg

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1 Precortalon Aquosum[?] kindly supplied by Pharmacia Ltd Uppsala Sweden Ewos Co Sodertalje Sweden

Radiography

The skeleton of each animal was examined radiographically under light ether anaesthesia at the beginning and end of the experimental period Each rat was placed with the spinal column and the extremities fixed directly on an X ray film The same exposure conditions film and developer were used throughout

Measurement of the cortical thickness of the mid shaft of the femur

This was performed after division of the bone at the middle of the diaphysis (± 0 5 mm) perpendicular to its long axis The internal and external transverse diameters were carefully measured with the aid of a vernier caliper at the four cut surfaces of the two divided femora of each animal Mean values were used The cortical thickness at this point was calculated as the difference between the external and the internal diameter and with an accuracy of 0 05 mm This figure was divided by the value for the external transverse diameter of the shaft at the same level and this fraction was multiplied by 100 In this way the femoral score was calculated according to *Barnett and Nordin* (1960)

Ash determinations

The ash content of the whole right tibia including the bone marrow and articular cartilages was determined as described previously (*Larsson* 1969 a) and was expressed as per cent of the wet weight

Hydroxyproline determinations

The hydroxyproline content of the whole third metacarpal bone including the bone marrow and the articular cartilages was determined by the method of *Neuman and Logan* (1950) All bones within the whole series were dried simultaneously at 45 C for 24 hours and were then weighed in weighing containers Protein hydrolysates were prepared by autoclaving the whole bone with 0 5 ml of 6 N hydrochloric acid in sealed tubes for 10 hours at 100 C Duplicate determinations were performed throughout and the mean value was used The coefficient of variation for these analyses was 2 0 per cent

Density of the dried humerus

The density of the dried whole bone including the bone marrow and articular cartilages was determined according to the method of *Robinson and Elliott* (1957)

Preparation of undecalcified sections

The first tail vertebra of all the rats was freed of most of the surrounding soft tissues and then fixed and dehydrated in 6 changes of 96 per cent alcohol for 6 days The specimens were embedded in methacrylate as described earlier (*Larsson* 1969 a) Using a fine bandsaw the trimmed plastic blocks were cut into sections approximately 0 5 mm thick and exactly perpendicularly to the long axis of the vertebra

Quantitation of the amount of vertebral bone

Quantitative determination of bone present in a standard area was performed as follows Undecalcified methacrylate embedded sections from the first tail vertebra were ground first on an oscillating grinder and then by hand to a thickness of approximately 50 μ Only that section which contained most of the transverse processes was examined unstained with the aid of an integrating eyepiece (Zeiss I) as described by *Wagner* (1965) The number of vertebral bone hits of 200 points was determined with the point network exactly in the centre of the section at a linear magnification of 30 ×

Microradiography

Of all the animals undecalcified methacrylate embedded cross sections from the second tail vertebra were ground on a Knuth Rotor grinder to a thickness of approximately 80 μ with water as a lubricant and using Silicone Carbide papers Nos 220 and 600 The sections were radiographed on Kodak MR plates in a Philips PW 1009 apparatus The procedure was the same as described previously (*Larsson* 1969 a)

Tetracycline labelling

All animals were labelled with chlortetracycline (Aureomycin© Lederle) in 2 doses of 20 mg per kg body weight administered by intraperitoneal injection 10 and 20 days before sacrifice Approximately 60 μ thick undecalcified methacrylate embedded cross sections from the second tail vertebra were mounted under coverslips in fluorescence free balsam (Permount) and were examined in a fluorescence microscope (Zeiss) fitted with an UV High Pressure Vacuum lamp HBO 200 with exciter filters UG 2 and UG 5 and barrier filters 65 and 41

Prepar ion of decalcified sections

The third tail vertebra of all animals was fixed in 10 per cent neutral formalin for 24 hours and then decalcified for 12—14 days in a mixture of equal parts of 20 % monosodium citrate and 44 % formic acid The specimens were then immersed in 5 per cent disodium sulphate for 24 hours washed with water for 24 hours and dehydrated by successive immersion in 70 per cent 95 per cent and absolute alcohol (2 changes) The specimens were then immersed first in methyl benzoate and then in xylol and were finally embedded in paraffin Sections 5 μ thick were cut and were stained with Ehrlich s haematoxylin and eosin and in addition azocarmine G Adjacent sections were also stained with an 0 5 per cent solution of toluidine blue in phthalate at pH 4 4 as described by *Belanger and Hartnett* (1960)

Preparation of histological sections of the adrenals

The adrenal glands from the normal controls and the animals treated for 14 and 16 weeks were fixed in 10 per cent neutral formalin embedded in paraffin and cut into sect ons 5 μ thick Representative sections were stained with Ehrlich s haematoxyl n and eosin

Statis ical tre tment of da a

The analytical data obtained from the rats in each group were subjected to analysis of variance with one way lay out according to *Scheffe* (1961) The hypothesis of no difference between groups was tested at the 5 per cent significance level When a significant result was obtained data of one or more groups were combined in order to find significant contrasts These were tested according to *Scheffe* (1961) In the present study the term significant stands for statistically significant as found with the tests described above

RESULTS

All animals survived the treatment except one This animal was sacrificed because of a parotid tumour and was excluded No infections or any other intercurrent diseases occurred The normal control animals showed a slight in rease in body weight by 5 to 7 per cent during the first 6 weeks Subsequently

Groups		No of animals	Initial body weight grams	S E M	No of animals	Final body weight grams	S E M
Normal controls		5	335 8	6 0	5	312 4	4 2
Ooph + prednisolone for	1 week	5	359 5	7 2	4	285 6	5 3
	2 weeks	5	354 6	10 4	5	285 6	9 7
	3	5	359 3	7 0	5	271 5	8 7
	4	5	338 5	7 3	5	289 5	13 6
	5	5	360 2	9 7	4	283 0	13 0
	8	5	358 2	7 2	5	270 0	10 4
" ,	, 10	5	338 8	5 2	4	265 4	5 6
" ,	12	5	343 4	5 2	4	257 3	9 6
,	14	5	327 4	7 3	5	263 8	14 7
,	16	5	362 2	11 6	5	252 9	8 9
			F = 2 43 sign			F – 2 95 sign	
			$F_{0.05}$ (10 44) = 2 05			$F_{0.05}$ (10 40) = 2 08	

Table I a The initial and final body weights of normal control rats and oophorectomized rats treated with prednisolone for different periods of time (S E M =standard error of the mean)

until the end of the 16th week the body weight remained unchanged *All the* experimental animals showed a considerable loss of body weight (Table 1 a b *Fig 1*) *During the first 3 weeks of prednisolone treatment there was a decrease in* body weight by approximately 20 *per cent* after which there was a further decrease by 10 per cent of the initial value The estimated food consumption was found to be slightly less than normal during the first 2 weeks of prednisolone treatment Subsequently there was no appreciable change in food intake in relation to body weight Considerable depletion of the adipose and muscle tissues and atrophy of the skin occurred in all corticosteroid treated animals Otherwise the animals were in good health and moved about freely in their cages

Weeks	Normal controls %	S E M	Oophorectomy + Prednisolone %	S E M
1	4 0	0 90	13 6	1 90
2	4 4	1 39	17 9	2 19
3	- 0 5	2 22	- 19 4	1 67
4	3 0	1 62	- 20 4	1 96
5	[illegible]9	1 70	- 21 5	1 73
6	5 1	2 29	- 19 7	1 87
7	8 3	1 39	- 19 7	1 41
8	7 9	1 51	- 20 2	1 74
9	7 8	2 43	- 18 7	1 77
10	7 3	1 54	- 21 8	1 70
11	5 9	2 01	- 24 2	1 71
12	7 4	1 [illegible]3	- 27 6	2 06
13	7 [illegible]	1 16	26 8	1 46
14	6 1	0 58	- 27 0	1 42
15	5 9	1 35	- 28 3	2 00
16	5 4	1 32	- 30 1	2 08
	F = 3 71 sign		F = 6 27 sign	
	F_0 (15 64) = 1 84			

Table 1 b The percentage change in body weight of the initial value *in normal* control rats and in oophorectomized rats treated with *prednisolone* for 16 weeks

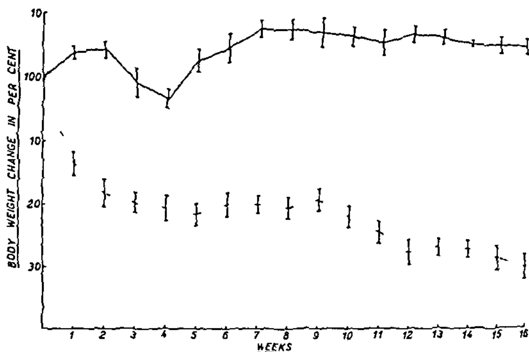


Fig 1 Body weight change in per cent of the initial weight in normal control rats (whole line) and in oophorectomized rats treated with prednisolone for 16 weeks (broken line) The bars represent the standard error of the mean

The length of the femur showed no significant difference between the normal control group and the groups of oophorectomized rats treated with prednisolone for 1 to 16 weeks

Histological examination of the ovaries removed from ten animals revealed both primary and secondary follicles in all specimens

Radiography

The radiograms of the skeleton showed closed epiphyseal zones in all animals at the start of the experimental period On comparison of the radiograms obtained at the start and a the end of the experimental period no noteworthy changes in the calcification of the skeleton were observed in any of the animals

Cortical thickness at the mid shaft of the femur (Table 2)

In the ten groups of oophorectomized rats treated with prednisolone for 1 to 16 weeks consistently lower mean values were found when compared with that of the normal control group. In the groups treated for 8 and 16 weeks respectively the calculated femur score was significantly lower than that of the control group. The mean values of the nine groups of rats treated for 2 to 16 weeks were approximately 10 to 20 per cent lower than that of the control group.

Groups		No of animals	Femur score	S.E.M.
Normal controls		5	43.5	2.02
Ooph + prednisolone for	1 week	5	39.9	2.13
	2 weeks	5	37.0	1.27
,,	3	5	36.6	1.56
	4	5	35.4	0.73
	5	5	37.3	1.41
	8	5	34.3	0.54
	10	5	38.4	1.03
	12	4	35.8	0.79
	14	5	37.7	0.71
,,	16	5	33.3	1.76
			F = 4.07 sign	
			$F_{0.05}$ (10,43) = 2.06	

Table 2 The femur score in normal control rats and in oophorectomized rats treated with prednisolone for different periods of time

Percentage of vertebral bone hits (Table 3)

Compared with the control group consistently lower mean values were found in all experimental groups. The three groups of rats treated for 12 to 16 weeks showed mean values 15 to 18 per cent lower than that of the normal controls. This difference was not significant however.

Groups	No of animals	% Hits	S E M
Normal controls	5	40 1	1 03
Ooph + prednisolone for 1 week	4	34 0	3 87
, , 2 weeks	5	36 2	2 26
" , " 3 ,	5	32 9	2 75
" " 4	5	38 1	1 79
, , , 5	5	35 0	1 97
, " , 8 ,	5	40 4	1 59
, " 10 ,	5	37 6	1 55
, " " 12 ,	4	32 3	3 20
, 14 ,	5	33 9	1 78
" , , 16	5	34 9	2 27
		F = 1 55 n s	
		$F_{0\ 95}$ (10 42) = 2 06	

Table 3 The percentage of vertebral bone hits in normal control rats and oophorectomized rats treated with prednisolone for different periods of time

Groups	No of animals	% Ash	S E M	
Normal controls	5	50 4	0 39	
Ooph + prednisolone for 1 week	5	47 7	0 41	
, 2 weeks	5	47 8	0 51	
, 3	5	49 5	0 66	
" 4	5	48 4	0 46	
" 5	5	49 4	0 68	
, 8	5	48 0	0 63	
10	5	49 7	0 69	
" 12	4	48 9	0 41	
, 14	5	47 4	0 60	sign
, 16	5	47 2	0 51	sign
		F = 3 64 sign		
		$F_{0\ 95}$ (10 43) = 2 06		

Table 4 The percentage ash content of the whole tibia in normal control rats and in oophorectomized rats treated with prednisolone for different periods of time

Ash content of the whole tibia (Table 4)

The two groups of oophorectomized rats treated with prednisolone for 1 and 2 weeks showed values approximately 5 per cent lower than those of the normal control group. This difference was not significant, however. Only slightly decreased values were found in the six groups of rats treated with prednisolone for 3 to 12 weeks. The two groups of rats treated with prednisolone for 14 and 16 weeks showed values more than 6 per cent lower than those of the control group. This difference was significant.

Hydroxyproline content of the metacarpal bone (Table 5)

All the experimental groups showed mean values which were consistently lower than that of the control group. These differences were not significant, however.

Groups		No of animals	‰ Hydroxy proline	S E M
Normal controls		5	26.1	0.38
Ooph + prednisolone for	1 week	5	25.6	0.60
" "	2 weeks	5	24.7	1.02
	3	5	24.5	0.67
	4	5	25.3	0.56
"	5	5	24.5	0.62
" "	8	5	25.0	0.57
	10	5	25.5	0.44
"	12	4	25.5	0.86
" "	14	5	24.5	0.42
	16	5	25.0	0.39
			F = 0.73 n.s	
			$F_{0.05}(10,43) = 2.06$	

Table 5 The promille hydroxyproline content of the metacarpal bone in normal control rats and in oophorectomized rats treated with prednisolone for different periods of time

Density of the dried humerus (Table 6)

All the experimental groups except the group treated for 2 weeks showed mean values which were consistently lower than that of the control group These differences were not significant however

Groups			No of animals	Density	S E M
Normal controls			5	2 34	0 040
Ooph + prednisolone for	1	week	5	2 23	0 069
,, ,,	2	weeks	5	2 33	0 092
,,	3	,,	5	2 20	0 106
,, ,,	4		5	2 18	0 022
,, ,,	5		5	2 08	0 075
,, ,,	8		5	2 16	0 109
,, ,, ,,	10		5	2 24	0 111
,, ,, ,,	12		4	2 16	0 028
,,	14		5	2 10	0 039
,, ,,	16		5	2 14	0 104
				F = 1 09 n s	
				$F_{0\ 95}$ (10 43) = 2 06	

Table 6 The gross bone density of the humerus in normal control rats and in oophorectomized rats treated with prednisolone for different periods of time

Microradiography

The microradiographs of undecalcified vertebral cross sections from the animals in the control group showed that both the cortical and the trabecular bone were evenly mineralized (Fig 2) In this nonlamellar (woven) bone there were no secondary osteones and no resorption cavities In all experimental animals microradiography showed that the cortical and the trabecular bone had the

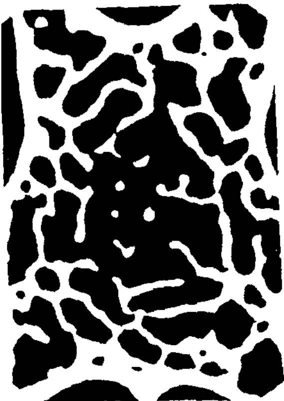


Fig. 2. Microradiograph of a cross section through the second tail vertebra of a normal rat. (x25)

same degree of mineralization and were as evenly mineralized as in the control animals. In the experimental animals the bone trabeculae appeared slightly thinner than in the normal controls but otherwise no differences were found (Fig. 3). No resorption cavities were seen.

Histological observations

In all animals decalcified cross sections of the third tail vertebra were stained with toluidine blue at pH 4.4 and in addition with haematoxylin eosin and azocarmine C. The sections were cut from parts of the vertebra chosen at random in the different animals. In each animal however all the sections were

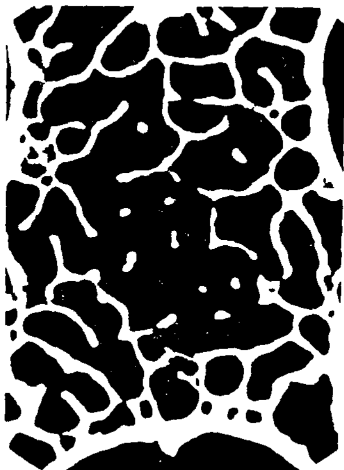


Fig 3 Microradiograph of a cross section through a corresponding part of the second tail vertebra of a rat after combined oophorectomy and prednisolone administration for 16 weeks The bone trabeculae are slightly thinner than normal (x25)

cut from the same part of the vertebra allowing adjacent sections to be examined after the three different staining proceduces

In both the cortical and the trabecular bone of the normal animals osteocytes with enlarged almost spherical lacunae were frequently found These osteocytes had often retracted to the lacunar wall and showed a pyknotic nucleus (Fig 4) Lacunae which were empty of cells were regularly found especially in the cortical bone mid way between the marrow cavity and the periosteum but often in the cortical bone layers nearest to the cavity and also in the bone trabeculae These lacunae and the canaliculi stained violet with haematoxylin eosin and were metachromatic with toluidine blue The immediate border of the osteocyte lacunae and the canaliculi stained violet with haematoxylin eosin and were metachromatic with toluidine blue This was often found also in lacunae empty of cells No osteoid tissue was observed nor osteoblasts or osteoclasts

Distinct areas showing slight basophilic staining with haematoxylin eosin were regularly found in the trabecular bone of the metaphyseal parts of the vertebra (Fig. 5). Nearer the midportion of the vertebra the basophilic areas decreased in frequency and were not seen in the cortical bone. They stained only faintly blue with azo carmine G and were located in the spaces intervening between parallel fibered bone staining deep blue (Fig. 6). These areas showing basophilic staining with haematoxylin eosin gave evident metachromasia with toluidine blue (Fig. 7).

In the experimental animals the same histological observations were made as in the normal controls. The osteocytes, the lacunae, the capsule of the lacunae and the *canaliculi had the same appearance and showed the same staining* properties in the prednisolone treated oophorectomized animals as in the controls. No difference in the frequency of hypertrophic osteocytes and lacunae empty of cells was observed. Neither were osteoid tissue, osteoblasts or osteoclasts

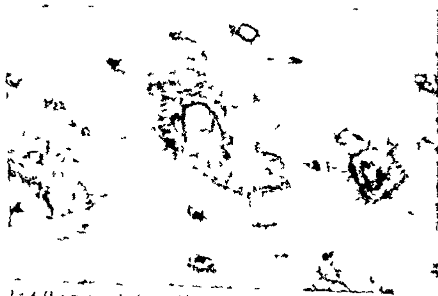


Fig. 4. [illegible] graph [illegible] cal bone from a vertebra of a normal rat. Osteocytes with enlarged lacunae can be seen. There are also *empty lacunae*. Haematoxylin eosin [illegible]

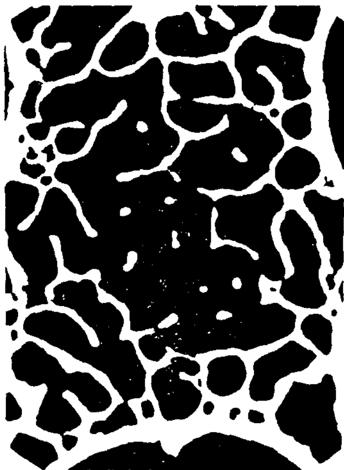


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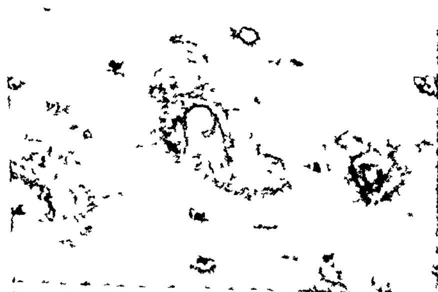


Fig. 4. Photomicrograph of cortical bone from a vertebra of a normal rat. Osteocytes with enlarged lacunae can be seen. There are also empty lacunae. Haematoxylin eosin (x5)



Fig 5 Photomicrograph of vertebral bone from a normal rat showing basophilic areas Haematoxylin eosin (x500)



Fig 6 Photomicrograph of an adjacent section of the vertebral bone shown in Fig 5 The basophilic areas are light and located *between the dark collagen* bundles Azocarmine G (x500)



Fig 7 Photomicrograph of an adjacent section of the vertebral bone shown in Figs 5 and 6 The basophilic areas show evident *metachromasia Toluidine* blue at pH 4 4 (x500)



Fig 8 Photomicrograph of vertebral bone from a rat treated with combined oophorectomy and prednisolone administration for 16 weeks Basophilic areas can be observed Haematoxylin eosin (x500)



Fig 9 Photomicrograph of an adjacent section of the vertebral bone shown in Fig 8 The basophilic areas located between the dark collagen bundles are stained only lightly or not at all Azocarmine G (x500)



Fig 10 Photomicrograph of an adjacent section of the vertebral bone shown in Figs 8 and 9 The basophilic areas show evident metachromasia There was no difference from the normal in the degree of metachromasia after treatment with combined oophorectomy and prednisolone administration for up to 16 weeks Toluidine blue at pH 4 4 (x5 0)



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Fig 8 Photomicrograph of vertebral bone from a rat treated with combined oophorectomy and prednisolone administration for 16 weeks. Basophilic areas can be observed Haematoxylin eosin (x5ᴗᴗ)



Fig 9 Photomicrograph of an adjacent section of the vertebral bone shown in Fig 8 The basophilic areas located between the dark collagen bundles are stained only lightly or not at all Azocarmine G (x5ᴗ0)



Fi 1^ Photomicrograph of n adjacent section of the ertebral bone shown in F s 8 and 9 The basophilic areas show evident metachromasia There was no difference from the normal n the degree of metachromasia after treatment with combined oophorectorry and prednisolone administration for up to 16 weeks Toluidine blue at pH 4 4 (x5 0)



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Fig. 17 Fluo ophotom crog aph of undecalcified sect on of ertebral bone from a rat treated with combined oophore tomy and prednisolone administration for 16 weeks There is only a th n fluorescent line after the 2 labellin s with chlortetracycline (x4)

Weight and histology of the adrenals (Table 7)

All the ten groups of oophore tomized rats treated with prednisolone for 1 to 16 weeks showed a decrease in the weight of the adrenals In the five groups of rats treated for 8 to 16 weeks the decrease was significant This also held when the weight of the adrenals was correlated to the body weight

Histological examination showed pronounced atrophy of the zona fasciculata in the corticosteroid treated animals

DISCUSSION

This study is concerned with the reaction of the well mineralized skeleton of one year old fully grown female rats to combined oophorectomy and prednisolone treatment for different periods of time It has been observed earlier that after



Fig 11 Fluorophotomicrograph of undecalficied section of vertebral bone from a normal rat Despite the time interval of 10 days between the 2 administered doses of chlortetracycline only one narrow fluorescent line can be seen (x400)

observed in the treated animals The areas showing metachromasia with toluidine blue *exhibited the same staining properties in corticosteroid treated as in normal* animals (Figs 8—10)

Fluorescence microscopy

In the normal animals fluorescence of newly formed bone was observed in only very few parts of the trabecular bone surfaces and on the surfaces of bone canals (Fig 11) Despite the time interval of 10 days between the two administered doses only one narrow fluorescent line was found These observations indicate that the rate of new bone formation in these old rats is very low In the experimental animals the fluorescent micrographs (Fig 12) were similar to those in the normal controls



F 12 Fluorophotomicrograph of undecalcified section of vertebral bone from a rat treated with combined oophore tomy and prednisolone administration for 16 weeks There is only a thin fluorescent line after the 2 labellings with chlortetracycline (x4)

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Groups		No of animals	Adrenal weight, mg	S E M	No of animals	Adrenal weight/body weight (x10—⁵)	S E M
Normal controls		5	51 8	4 09	5	16 6	1 26
Ooph + prednisolone for	1 week	4	36 2	4 90	4	12 6	1 48
	2 weeks	5	43 4	4 32	5	15 3	1 54
	3	5	42 7	5 77	5	15 8	2 19
	4	5	41 0	6 15	5	14 1	1 97
	5	4	38 5	5 29	4	13 8	2 14
	8	5	19 1	1 19	5	7 1	0 44
	10	4	17 1	4 14	4	6 4	1 46
	12	4	18 7	3 39	4	7 2	1 08
	14	4	15 8	0 81	4	5 9	0 54
	16	4	19 6	0 92	4	8 0	0 44
			F = 9 57 sign			F = 7 92 sign	

F_{05} (10 38) = 2 10

Table 7 Weight of the adrenals (mg) and weight of the adrenals/body weight (x10—⁵) in normal control rats and in oophorectomized rats treated with prednisolone for different periods of time

a certain age female rats attain a constant body weight (*Singer et al* 1952) This was found also in the present study in which the body weight of the normal control rats remained unchanged after about the 6th week of the experiment The radiological examination showed further that the skeletal growth was complete in all animals at the beginning of the experiment No significant difference in femur length was found between normal and experimental animals

In the present study oophorectomy was performed in order to reduce the endogenous oestrogens which are known to have a calcium retaining effect in contradistinction to the calcium wasting effect of corticosteroids (*Gordan et al* 1967) In addition to considerable depletion of adipose and muscle tissues and atrophy of the skin the effect of the treatment was manifested by pronounced atrophy of the adrenal cortex especially the zona fasciculata Rats treated with cortisone for 21 days show a selective depletion of lipid in the zona fasciculata and the zona reticularis whereas the zona glomerulosa becomes hypertrophied and full of lipid (*Wexler* 1963) This inactivity of the adrenal cortex induced by cortisone administration would mean a decrease not only of endogenous cortisone from the zona fasciculata but also of oestrogens and androgens from the zona reticularis Furthermore histological examination of the ovaries removed in the present experiment revealed both primary and secondary follicles These circumstances indicate that the experimental conditions of the present study induced the hormonal lack of balance which has been considered to cause senile osteoporosis in humans (*Reifenstein* 1957)

In an earlier experiment designed to study the effect on the skeleton of a hormonal disturbance similar to that in osteoporotic humans as reported by *Reifenstein* (1957) young male rats were deprived of endogenous adrenal corticosteroid and gonadal steroid hormones by total adrenalectomy and gonadectomy and were injected daily with cortison acetate in a dose of 7 mg per kg body weight (*Caldwell* 1962) There was radiographic evidence of osteoporosis after 100 days of cortisone treatment and after 160 days the ratio femoral calcium/wet weight showed a decrease by approximately 25 per cent In the adult oophorectomized rats studied in the present investigation no radiographic signs of osteoporosis were observed at any period of the prednisolone treatment The ash content of the whole tibia showed a slight decrease initially but no consistent change was observed subsequently in the rats treated for different periods of up to 12 weeks Thereafter a significant decrease by 6 to 7 per cent was noted in the two groups of rats treated for 14 and 16 weeks respectively Histological examination of decalcified sections and microradiographs of undecalcified vertebral sections showed no differences from the normal The

loss of bone minerals observed in the rats treated for 14 and 16 weeks therefore corresponds to osteoporosis as described by *Collins* (1966) This is supported by the fact that in a subsequent study (*Larsson and Vejlens* 1969) on the same material no si nificant change in the ash content of the compact bone was found in these animals The tendency to a decrease of the hydroxyproline content of the whole metacarpal bone observed in the present study also suggests a reduction of skeletal tissue The same tendency to slightly decreased values was found with regard to the cortical thickness of the mid shaft of the femur the percentage of vertebral bone hits and the density of the whole humerus Except for the femur score no significant differences were found with these methods which might have been due to greater methodological variations than for the ash determinations

In view of the considerable depletion of other tissues such as adipose and muscle tissues and the skin the skeletal tissue of the adult rat must be regarded as fairly stable to the action of combined oophorectomy and excess corticosteroids From results obtained in adult rats after cortisone treatment alone for up to 8 weeks the same conclusion concerning bone collagen was reached by *Sobel and Marmorston* (1954) These findings are in contradistinction to results concerning the young growing skeleton of the rat (*Storey* 1960 *Caldwell* 1962) and of the rabbit (*Sissons and Hadfield* 1957 *Storey* 1957 *deValderrama and Munuera* 1965) In rabbits al o the effect of corticosteroids on the adult skeleton is less pronounced than in young animals (*Storey* 1961)

It seems as if the hormonal disturbance induced in the experiment of *Caldwell* (1962) had a more pronounced effect on the skeletal tissue than that of the present study However in *Caldwell s* experiment young growing rats were used and the results of the two studies are therefore not comparable Thus combined adrenalectomy orchidectomy and cortisone treatment caused a pronounced interference with the normal skeletal growth and development Also in other experimental studies where young animals have been used the reported osteoporotic bone lesions induced by excess corticosteroids seem to have been mainly the result of inte ference with normal skeletal development In the present investigation on fully grown animals the hormonal disturbance exerted its effect on the maintenance of the mature skeletal tissue which is the essential problem in connection with the development of osteoporosis in humans

It has been proposed that senile osteoporosis develops as a result of inhibited protein synthesis of the bone matrix (*Reifenstein* 1957) There is experimental evidence that cortisone primarily reduces the synthesis of bone collagen and does not increase its degradation in the rat (*Smith and Allison* 1965) Results

obtained in studies of the metabolism of bone collagen following intraperitoneal injection of glycine 2 C^{14} in the rat indicate that a major proportion of bone collagen is synthesized at an early age and that the rate of metabolism of collagen in bone is an inverse function of age (*Kao et al* 1965) This means that the reaction of bone collagen to excess cortisone is more pronounced in young than in adult individuals Besides this inhibitory effect upon collagen synthesis the well documented calcium wasting effect of corticosteroids (*Gordan et al* 1967) may also be more pronounced in the growing skeleton not only because of the high rates of bone apposition and resorption in the young animal but also because of more extensive bone calcium exchange in the young than in the mature skeleton (*Leblond et al* 1950 *Tomlin et al* 1953) In humans adrenal steroids have been reported to produce osteoporotic bone lesions in children more frequently than in adults and generally after treatment on lower doses and in less time (*Schlesinger et al* 1961)

It has been found in experiments on young growing rats that calcium intake and changes in calcium metabolism may be of primary importance for the development of osteoporosis following corticosteroid therapy (*Storey* 1960) Young rabbits treated with cortisone and fed a low calcium diet develop osteoporosis associated with extensive osteoclastic activity and secondary hyperparathyroidism (*Storey 1961*) The experiment of *Clark and Roth (1961)* suggests that hydrocortisone decreases the reabsorption of calcium by the renal tubules in the adult rat This calcium wasting effect was also demonstrated in a study on the same material as used in the present experiment (*Larsson* 1969 b) The data obtained indicated increased mobilization of skeletal calcium for maintenance of the blood calcium level There was no consistent change in the calcium accretion rate of the bone The decrease in bone mass found in the present study therefore represents a considerable calcium loss and corresponds well with that observed in one year old male rats fed a low calcium diet (0 09 per cent calcium) for the same periods of time (*Larsson* 1969 a) In that experiment also a significant reduction of the ash content of the whole tibia by 6 to 7 per cent was noted after 14 and 16 weeks on a low calcium diet These findings suggest that changes in calcium metabolism and the efficiency of calcium homeostasis may be of major importance for the slight bone mass reduction observed after combined oophorectomy and prednisolone administration in the present study It is possible that a more significant reduction in bone mass might occur on extension of the duration of prednisolone treatment However it is conceivable that reduction in caloric intake might then occur and this alone can give rise to osteoporosis (*El Maraghi et al* 1965) In the present

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Histological examination of decalcified vertebral cross sections showed a regular frequency of distinct areas giving evident metachromasia with toluidine blue at pH 4 4 and located in spaces intervening between parallel fibered bone in the metaphyseal bone trabeculae and metaphyseal cortex These metachromatic areas contained only a small amount of collagen stainable with azocarmine G These areas seem to consist of intercellular acid mucopolysaccharides extending from the epiphyseal region inwards to the metaphysis and no such areas were observed in the diaphyseal cortex In the experimental animals no charge in staining properties of these areas was found It is well known that excess of corticosteroids decreases the synthesis of acid mucopolysaccharides in connective tissues and that the incorporation of S^{35} sulphate into chondroitin sulphate of costal cartilage in rabbits is diminished after corticosteroid treatment (*Bostrom and Odeblad* 1954 *Whitehouse and Bostrom* 1961) In one year old rats treated with cortisone acetate in doses of 15 to 18 mg/kg for up to 8 weeks a decrease in the hexosamine contents of the whole femur was found in contrast to unchanged collagen contents and it was suggested that a decrease of muco polysaccharides precedes the events which lead to the development of osteoporosis in Cushings disease (*Sobel and Marmorston* 1954) The changes observed may be unspecific with regard to the mucopolysaccharides of the bone tissue itself and no support for this theory can be obtained from the observations made in the present study This point is discussed further in a biochemical investigation (*Larsson and Vejlens* 1969)

The results of the present study show that the skeletal tissue of one year old rats is relatively stable to the action of combined oophorectomy and prednisolone administered for up to 16 weeks Despite a pronounced decrease in body weight there was only a slight but significant decrease of the bone tissue in animals treated for 14 and 16 weeks This may however correspond to a considerable calcium loss in view of the effect of corticosteroids on calcium metabolism and calcium homeostasis This is discussed further in a following study (*Larsson* 1969 b)

SUMMARY

In one year old rats the effect on the skeletal tissue of combined oophorectomy and prednisolone administration (7 5 *mg/animal/day Precortalon aq*) *for 1* to 16 weeks was studied This treatment caused considerable depletion of adipose and muscle tissues a total decrease in the body weight by 30 *per cent* and

investigation the experimental animals treated with prednisolone for 2 weeks and more showed no apparent difference in food consumption in relation to body weight compared with that of the normal controls It is therefore hardly likely that a reduced calcium intake would be responsible for the bone reduction observed after 14 and 16 weeks of treatment

Microscopic examination of decalcified sections of the vertebral bone from the normal adult female rats showed a high frequency of retracting osteocytes Enlarged spherical lacunae, entirely empty or containing a pyknotic nucleus were regularly found especially in the cortical bone These changes were unspecific and were found to the same extent in normal as in prednisolone treated oophorectomized animals Similar morphological changes have also been observed in aged humans and have been ascribed to physiologic aging of bone (*Sherman and Selakovitch* 1957) In patients with severe osteoporosis these changes are more pronounced (*Urist et al* 1963) The morphologic appearance of the bone observed in the present study did not seem to be related to the reaction of the bone tissue to the treatment given

In histological sections of vertebral bone tissue no osteoblasts or osteoclasts were found either in the normal or in the experimental rats A small amount of bone surface showing tetracycline labelling was the only sign of low osteoblastic activity No change was observed in the corticosteroid treated oophorectomized animals, in contrast to observations on growing animals in which excess corticosteroids regularly suppress osteoblast formation (*Stanisavljevic et al* 1962 *Hulth and Olerud* 1963) In addition on administration of high doses of cortisone acetate highly increased osteoclast formation has been observed in young rabbits (*deValderrama and Munuera* 1965) In humans with hyper corticoidism the reported bone changes are not quite conclusive Thus rarefaction of vertebral bone trabeculae with seemingly adequate numbers of osteoblasts and no evidence of osteoclastic resorption was reported by *Follis* (1951) Decreased formation and resorption of bone was reported by *Storey* (1963) Other investigators have deduced from histological (*Sissons* 1956) and micro radiographic (*Jowsey et al* 1965) studies that osteoporosis in human hyper corticoidism results from impaired new bone formation in the presence of normal or increased bone resorption Recently an elevated number of active osteoblasts and a high uptake of tetracycline have been observed in human hypercorticoidism and in severe cases high osteoclastic activity (*Birkenhager et al* 1967) While in young rats excess cortisone exerts a pronounced effect on the kinetics of the bone cell populations (*Simmons and Kunin* 1967) there was no such effect in the old rats used in the present study

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significant atrophy of the adrenal cortex (zona fasciculata) In spite of the extensive loss in body weight induced, the effect of the treatment on the skeletal tissue was moderate There were no roentgenological signs of osteoporosis In the groups of oophorectomized rats treated with prednisolone for 14 and 16 weeks a significant reduction of the ash content of the tibia was found while the groups of rats treated for shorter periods of time showed slightly but insignificantly lower values than those of the normal controls The cortical thickness of the mid shaft of the femur, calculated as the femur score also showed significantly decreased values There was also a slight, though not significant decrease in the percentage of vertebral bone hits' the hydroxyproline content of the metacarpal bone and the density of the humerus Microradiographs of undecalcified vertebral bone sections showed no changes in the degree of mineralization In the normal controls, histological examination of decalcified sections revealed a high frequency of retracting osteocytes in enlarged lacunae and lacunae which were empty of cells were regularly found Osteoblasts and osteoclasts were not seen and there was only a very small amount of vertebral bone surface showing tetracycline labelling Areas containing intercellular substance (acid mucopolysaccharides) giving metachromasia in toluidine blue were observed in the trabeculae of the vertebral bone In the experimental animals, the bone tissue showed the same morphological appearance as in the normal controls The areas containing acid mucopolysaccharides showed the same staining properties as in the normal animals No notable difference in tetracycline labelling was found The observed tendency to reduced bone mass is discussed with regard to the development of osteoporosis

ACKNOWLEDGEMENTS

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Studies on the Development of Experimental Osteoporosis

IV The Effect of Combined Oophorectomy and Prolonged Prednisolone Administration on the Blood Calcium Level and the Distribution of Ca^{45} between Blood and Bone in Adult Rats

by

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In young rats cortisone osteoporosis similar to that in rabbits has been reported by *Storey* (1960). It was shown that bone rarefaction occurred only when the rats were fed a diet in which the calcium and phosphorus contents were normal, i.e. 1.0 and 0.6 per cent respectively, or lowered; on a high calcium-phosphorus intake there was an increase in the density of the metaphyseal bone. This difference in the reaction of the bone to cortisone was believed to be associated with the well developed adaptive calcium metabolism of the rat. It has been known for many years that corticoids exert considerable influence on the calcium metabolism. The skeletal retention of bone seeking isotopes has been claimed to be inhibited by the administration of corticoids to rats (*Clark et al* 1959, *Milhaud et al* 1960, *Bohr and Dawids* 1964). Calcium excretion has been found consistently to be increased, but there is disagreement concerning the effect on intestinal calcium absorption. Young male rats subjected to bilateral adrenalectomy and orchidectomy are more sensitive to cortisone and develop osteoporosis despite a high calcium intake (*Caldwell* 1962). Oestradiol cured the osteoporosis in these animals despite continuous cortisone administration, whereas only very slight improvement was noted in animals given testosterone.

The present study is a continuance of a previous investigation (*Larsson* 1969 a) and was undertaken in order to obtain some information regarding the pathomechanism underlying the observed significant reduction of bone mineral caused by the hormonal imbalance induced in adult rats by oophorectomy combined with prolonged prednisolone administration. The data to be reported here concern the effect on the blood calcium level, the distribution of Ca^{45} between blood and bone and the calcium accretion rate of the bone in the same material of oophorectomized rats kept on prednisolone treatment for different periods from 1 up to 16 weeks.

MATERIAL AND METHODS

MATERIAL

Fifty five adult female rats of the Sprague Dawley strain[1] were used. All animals were stated to be 11 1/2 to 12 months old at the start of the experiment and had a mean initial body weight of 349.5 ± 2.7 grams. The animals were divided at random into ten experimental groups and one control group of 5 rats each. The experimental animals were oophorectomized via a midline

[1] Anticimex Co., Stockholm.

Treatment with glucocorticoids causes both a negative calcium balance and loss of bone in adult humans (*Albright and Reifenstein* 1948) The pathomechanisms involved during the development of the corticosteroid induced osteoporosis are still poorly understood however The antianabolic effect of glucocorticoids on connective tissues is well known and it has been proposed from histological observations that the decrease in the amount of bone tissue in humans with Cushing s syndrome is the result of inhibited new bone formation (*Sissons* 1956) It has also been pointed out from quantitative histological studies of rib sections that bone formation is profoundly depressed in cort coid treated patients and that bone resorption also appears to be depressed but to a lesser degree than the formation (*Villanueva et al* 1966) With the aid of quantitative microradiography of sections from the iliac crest decreased bone formation and increased resorption have been demonstrated both in Cushing s syndrome and after corticosteroid therapy (*Jowsey et al* 1965) The results obtained with the aid of bone seeking isotopes or stable strontium are not quite conclusive with regard to the effect of corticosteroids on the skeletal tissue Measurements of the bone mineralization rate by a variety of techniques have failed to find any consistent difference in this respect between normal and steroid treated individuals (*Nord n et al* 1963 *Nordin et al* 1964) Studies by means of stable strontium of a large number of patients taking synthetic steroids have revealed an increase in urinary excretion and bone accretion rate however in three cases of Cushing s syndrome small pool sizes and low turnover rates were found (*Gordan and Eisenberg* 1963) From strontium kinetic studies on corticoid treated osteoporot c patients it has been concluded that the bone accretion is normal or even increased and that the eventual decrease in bone mass is caused by accelerated bone resorption (*Eisenberg* 1966)

Osteoporosis similar to that in humans has been induced experimentally in young rabbits by excess cortisone (*Sissons and Hadfield* 1955 *Storey* 1957) The conclusion was drawn from histological studies that the bone rarefaction is the result of inhibited bone formation with an unopposed continuance of bone resorption (*Sissons and Hadf eld* 1955 *Sissons* 1956) It has also been deduced from observations based on histological studies in young rabbits that cortisone osteoporosis results not only from a cessation of bone formation but primarily from a direct degrading effect which causes a massive resorption of bone (*deValderrama and Munuera* 1966)

Determination of the Ca^{45} activity of the bone

The whole right tibia including the bone marrow and the articular cartilages was carefully freed of surrounding soft tissues and periosteum All bones were ashed simultaneously in a muffle furnace at 700°C for 16 hours, after which the ash weight was recorded with the aid of a Mettler balance and with an accuracy of 0 05 mg All ashed bones were then dissolved in 5 0 ml of 1 2 N HCl in 100 ml volumetric flasks When the ash was completely dissolved the flasks were filled to the mark with deionized water An aliquot of 2 0 ml from the final solution was transferred into a 25 ml polyethylene counting vial which was filled with a gel scintillator composed of 2 5 Diphenyloxazole (PPO) 1 0 g 1 4 bi 2 (4 Methyl 5 Phenyloxazolyl) Benzene (POPOP) 0 3 g Naphtalane 100 0 g Dioxan 1 litre and thixotrophic gel powder (CAB O SIL) to saturation

Determination of the Ca^{45} uptake of pure compact bone tissue

Acetone dried bone powder was prepared from the tubular bones as described elsewhere (*Larsson* 1969 b) Approximately 100 mgs of bone powder were ashed at 700°C in a muffle furnace for 16 hours The exact ash weight was then recorded after which the ash was dissolved in 2 0 ml of 1 2 N HCl directly in the counting vials After addition of the scintillator counting was performed

C^{45} activity of plasma

This was determined directly using 1 0 ml of plasma collected at sacrifice and about 0 2 ml of plasma obtained from the tail blood collected at different intervals after the administration of the isotope This procedure was considered suitable for the purpose of the present study (see *Budy* 1963) and has been recommended by *Kumar* (1966) The same scintillator was used as for the bone ash solutions

Calcium determination of the plasma

This was performed by flame photometry using an Fpendorf photometer on plasma collected at sacrifice Duplicate determinations were always performed The error of the method was found to be less than 1 per cent

Calcium content of the cortical bone powder

This was determined by atomic absorption spectrophotometry using an automated Perkin Elmer Model 303 Instrument as described elsewhere (*Larsson* 1969 b)

abdominal incision under ether anaesthesia All the animals recovered very quickly after the operation From the third day after oophorectomy each animal received 2 5 mg prednisolone[1] daily, dissolved in their drinking water This was supplied intermittently in such a way that the prednisolone was consumed during the following 1 — 2 hours The periods of prednisolone treatment varied from 1 up to 16 weeks The *control* group consisted of *normal* rats and was observed for 16 weeks The experimental and the control animals received the same ordinary laboratory food ration[2] and tap water *ad libitum* although, as mentioned above, the experimental animals were given their drinking water more intermittently Chemical analyses showed that the total calcium and phosphorus in this diet amount to 1 0 and 0 55 per cent respectively All animals were housed in individual cages in a separate room and were not exposed to sunlight The animals could move around freely in their cages

INVESTIGATIONAL PROCEDURES

A detailed description of the procedures used has been given in a previous paper (*Larsson* 1969 b) The body weight of each animal was recorded weekly The series was planned so that all the animals were sacrificed at the same time Seventy two hours before sacrifice 20 microcuries of Ca^{45}* in 1 0 ml physiolog cal saline solution were injected intraperitoneally in each animal All administered solutions were prepared from a single batch of $Ca^{45}Cl$ At intervals of 6 24 and 48 hours after the isotope injection 0 4 to 0 5 ml tail blood was collected and after 72 hours the animals were sacrificed by bleeding to death from the femoral artery under ether anaesthesia The blood samples obtained at 6 and 48 hours after the Ca^{45} injection were taken from three animals of each group and at 24 hours from the remaining two The collected blood was centrifuged immediately at 3 000 r p m for 15 minutes and the plasma transferred into acid washed test tubes and kept at - 20°C for later determinations of Ca^{45} activity The whole animal bodies were kept at - 20°C pending th subsequent bone preparations

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1 Precortalon Aquosum○ kindly supplied by Pharmacia Co Uppsala

2 Ewos Co, Sodertalje

* Calcium chloride in aqueous solution 2—5 c/g Ca C E S 2 The Radiochemical Centre Amersham, England

significance level When a significant result was obtained data of one or more groups were combined in order to find significant contrasts These were tested according to *Scheffe* (1961) In the following the term significant will stand for statistically significant *as found with the tests described above*

RESULTS

All animals survived except one which was excluded The normal control rats showed a slight initial increase in body weight but after 6 weeks the body weight remained at a constant level of 5 to 7 per cent above the initial value *The group of oophorectomized animals maintained on prednisolone treatment* for 16 weeks showed a total loss of body weight by approximately 30 per cent of the initial value A considerable depletion of the adipose and muscle tissues was observed in all experimental animals but otherwise the animals were in good condition No infections or any other intercurrent diseases were observed

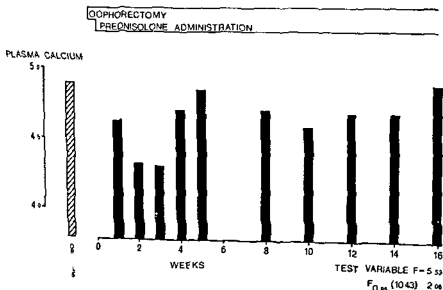


Fig 1 Plasma calcium in normal control rats and oophorectomized rats treated with *prednisolone* for different periods of time

For suppression of the interference by phosphorus lanthanum chloride was added to the solutions as recommended by *Willis* (1961) The added calcium recovery in these bone ash solutions was found to be 98 per cent Duplicate determinations were performed throughout The coefficient of variation for these analyses was less than 1 per cent

Ca^{45} activity determinations

These were performed with the aid of a Packard Tri Carb Liquid Scintillation Spectrometer[1] Corrections were made for background and decay It was not considered necessary to introduce any corrections for self absorption because of the constancy of counting efficiency

Treatment of isotope data

The Ca^{45} activity of bone was expressed as counts per minute per milligram of ash No significant difference was found in the calcium content of ash obtained from pure cortical bone tissue of the normal and the treated animals the mean calcium content was 38 09 ± 0 20 per cent Therefore the expression c p m per milligram of ash is equivalent to the specific activity and the factor 0 3809 was used when the bone accretion rates were calculated (see below) The Ca^{45} activity of plasma at 72 hours after the isotope injection was expressed as c p m per milligram of calcium The plasma Ca^{45} activity curves (Fig 2) were also based upon values expressed as c p m per milligram of calcium Because of the necessity for collecting as little blood as possible at the different periods after the administration of Ca^{45} calcium determinations were only performed on blood samples obtained at sacrifice

The accretion rates for the whole tibia expressed as mg calcium/hour/mg calcium of the tibia were calculated according to *Bauer et al* (1955) The mean values within each group were used throughout

Statistical treatment of data

The analytical data obtained from the rats in each group were subjected to analysis of variance with one way lay-out according to *Scheffe* (1961) The hypothesis of no difference between groups was tested at the 5 per cent

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1 Model 314 EX 2 Packard Instrument Company LaGrange Ill USA

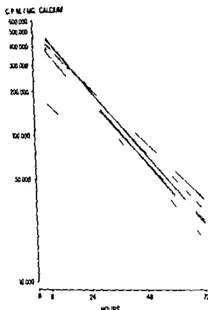


Fig 2 Plasma Ca^{45} specific activity corrected for body weight at 6 24 48 and 72 hours after the isotope injection in normal control rats (broken line) and in oophorectomized rats treated with prednisolone for different periods of time (whole line) Each dot represent the mean value for the control group

the normal control group At 24 48 and 72 hours after the administration of the isotope the plasma Ca^{45} activity showed consistently lower values in the experimental animals than in the normal controls

Plasma Ca^{45} specific activity at 72 hours after the Ca^{45} injection (Fig 3 Table 2)

In comparison with the normal control group lower values were obtained in the group of oophorectomized rats treated with prednisolone for 1 week. This difference was not significant however The two groups of animals treated for 2 and 3 weeks showed approximately the same values as the controls In all the seven groups of oophorectomized rats kept on prednisolone treatment for 4 to 16 weeks consistently decreased values were noted In these groups the plasma Ca^{45} activity was approximately 40 per cent lower than in the normal control group When the combined values for these groups were tested against those of the normal control group the difference was found to be significant.

Plasma calcium (Fig 1, Table 1)

The values of the oophorectomized rats treated with prednisolone for 1 2, 3 and 4 weeks were consistently lower than those of the control animals In the groups of rats treated for 2 and 3 weeks the fall in plasma calcium was significant and amounted to approximately 12 per cent The group of animals treated for 5 weeks showed normal values but, again, subnormal values were recorded in the four groups of oophorectomized rats maintained on prednisolone treatment for 8 10, 12 and 14 weeks This decrease was not significant, however Finally normal plasma calcium values were found in the group of animals treated for 16 weeks

Groups	No of animals	Plasma calcium mEq /l	S E M	
Normal controls	5	4 9	0 07	
Ooph + prednisolone for 1 week	5	4 6	0 10	
" , , 2 weeks	5	4 3	0 08	sign
" " , 3	5	4 3	0 03	
" " , 4 ,	5	4 7	0 08	
" " " 5 ,	5	4 9	0 08	
" " " 8 ,	5	4 7	0 02	
" " " 10 ,	5	4 6	0 09	
" " , 12 "	4	4 7	0 04	
" " 14 ,	5	4 7	0 14	
" " " 16	5	4 9	0 05	
		F = 5 53 sign		
		$F_{0\,95}$ (10 43) = 2 06		

Table 1 Plasma calcium in normal rats and oophorectomized rats treated with prednisolone for different periods of time (S E M = standard error of the mean)

Plasma Ca^{45} activity at different periods after the Ca^{45} injection (Fig 2)

In all groups of oophorectomized rats treated with prednisolone for different periods of time there was a more rapid fall in plasma Ca^{45} activity than in

Ca^{45} activity of the tibia 72 hours after the Ca^{45} injection (Fig 4 Table 3)

Slightly higher values were obtained in the groups of oophorectomized rats treated with prednisolone for 1 and 2 weeks compared with those of the normal controls This difference was not significant, however In the group of oophorectomized rats treated for 3 weeks the values obtained showed no difference from those of the normal controls In the groups of oophorectomized rats treated for 4 to 16 weeks successively lower bone Ca^{45} activity values we e .ot d, decreasing with the duration of prednisolone treatment When the combined values of the five groups of rats treated for 8 to 16 weeks were tested against those of the normal controls and the four groups of rats treated for 1 to 4 weeks the difference was found to be significant. In the groups of rats treated for 14 to 16 weeks the values were approximately 30 per cent lower than those of the normal controls

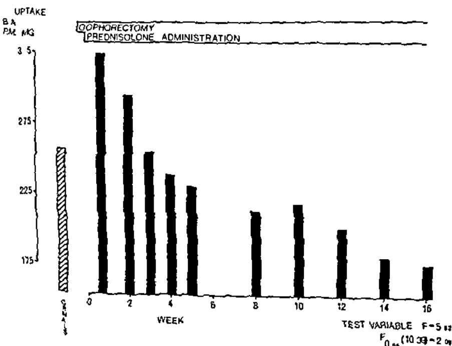


Fig 4 The uptake of Ca^{45} by the tibia 72 hours after the intraperitoneal administration of 0 microcuries of Ca^{45} per animal in normal control rats and oophorectomized rats treated with p ednisolone for different periods of time

Ca[45]—ACTIVITY
CPM/MG CALCIUM

OOPHORECTOMY +
PREDNISOLONE ADMINISTRATION

50 000
40 000
30 000
20 000

NORMALS

0 2 4 6 8 10 12 14 16
WEEKS

TEST VARIABLE F = 8 62
$F_{0\,95}$ (10 37) 2 10

Fig 3 Plasma Ca^{45} specific activity 72 hours after the intraperitoneal administration of 20 microcuries of Ca^{45} per animal in normal control rats and oophorectomized rats treated with prednisolone for different periods of time

Groups		No of animals	Plasma Ca^{45} c p m /mg calcium	S E M	
Normal controls		5	44597	2037	
Ooph + prednisolone for	1 week	3	32189	2457	
„	2 weeks	4	47847	5556	
„	3	4	42621	5436	
„	4	5	28202	3125	Sign
„	5	3	28156	208	
„	8	5	28856	2124	
„	10	5	27839	1188	
„	12	4	29253	2233	
„	14	5	27379	1497	
„	16	5	22326	1821	

$F = 8\ 62$ sign
$F_{0\,9}$ $(10\ 37) = 2\ 10$

Table 2 Plasma Ca^{45} specific activity 72 hours after the intraperitoneal injection of 20 microcuries of Ca^{45} per animal in normal control rats and oophorectomized rats treated with prednisolone for different periods of time

Ca^{45} activity of compact bone powder 72 hours after the Ca^{45} injection (Table 4)
Approximately the same values were obtained for the three groups of oophorectomized animals treated with prednisolone for 1 2 and 3 weeks as for the normal control group In the seven groups of rats treated for 4 to 16 weeks consistently lower values were obtained with a maximum decrease in the groups treated for 12 14 and 16 weeks When the combined values of the five groups of rats treated for 8 to 16 weeks were tested against those of the normal controls and the four groups of rats treated for 1 to 4 weeks the difference was found to be significant

Groups		Accretion rate (mg Ca/hour/mg Ca of the tibia)
Normal controls		$5\ 63 \times 10^{-}$
Ooph + prednisolone for	1 week	$7\ 52 \times 10^{-}$
	2 weeks	$5\ 93 \times 10^{-}$
	3	$5\ 08 \times 10^{-5}$
"	4	$5\ 14 \times 10^{-}$
"	5	$5\ 33 \times 10^{-5}$
	8	$5\ 98 \times 10^{-}$
	10	$5\ 01 \times 10^{-5}$
" "	12	$5\ 59 \times 10^{-5}$
" "	14	$4\ 18 \times 10^{-5}$
" "	16	$8\ 20 \times 10^{-5}$

Table 5 The mean calcium accretion rate for the tibia in normal control rats and oophorectomized rats treated with prednisolone for different periods of time

Calcium accretion rate for the tibia (Table 5)
This was calculated as mg calcium/hour/mg calcium of the tibia In the groups of oophorectomized rats treated with prednisolone for 1 and 2 weeks higher mean values were obtained than in the normal control group The six groups of rats treated for 3 to 12 weeks showed *approximately the same values* as that of the normal control group In the group of rats treated for 14 weeks a lower accretion rate was found while the group of rats treated for 16 weeks showed a higher accretion rate ompared with the control group

Groups	No of animals	Ca⁴⁵ activity c p m /mg ash	S E M	
Normal controls	5	257 4	11 7	
Ooph + prednisolone for 1 week	5	325 4	33 5	
„ , , 2 weeks	4	295 9	31 4	
„ „ , 3 ,	5	256 0	7 3	
„ , „ 4 ,	5	240 2	20 2	
„ , „ 5 ,	3	232 0	20 5	Sign
„ , , 8 „	5	215 0	14 8	
, 10	4	219 5	12 3	
, „ 12	4	202 9	5 0	
, , , 14	5	183 1	11 6	
, , , 16	5	177 9	18 9	

F = 5 82 sign

$F_{0\,95}$ (10 39) = 2 09

Table 3 The Ca^{45} uptake of the tibia (c p m./mg ash) 72 hours after the intraperitoneal injection of 20 microcuries of Ca^{45} per animal in normal control rats and oophorectomized rats treated with prednisolone for different periods of time

Groups	No of animals	Ca⁴⁵ activity c p m /mg ash	S E M	
Normal controls	4	44 6	4 0	
Ooph + prednisolone for 1 week	3	45 7	10 3	
, , 2 weeks	4	46 0	5 9	
, 3	5	44 2	1 9	
, , 4	5	36 0	2 1	
, „ 5	3	33 1	1 4	Sign
8	5	31 2	1 7	
, 10	4	35 7	2 6	
12	4	26 2	2 5	
, 14 ,	5	29 8	1 5	
, 16	5	28 0	2 4	

F = 4 68 sign

$F_{0\,95}$ (10 36) = 2 11

Table 4 The Ca^{4} uptake of compact bone (c p m./mg ash) 72 hours after the intra peritoneal injection of 20 micro uries of Ca^{45} per animal in normal control rats and oophorectomized rats treated with prednisolone for different periods of time

there is a tendency towards hypercalcemia (*Walser et al* 1963) and that cortisone tends to reverse the hypercalcemia accompanying different diseases such as sarcoidosis and hypervitaminosis D (*Dent 1956 Connor et al* 1956) Adrenalectomy further gives rise to increased concentrations of blood calcium in dogs (*Rogoff and Stewart* 1928) rabbits (*Kisch* 1924) and rats (*Rohdenburg and Krebbiel* 1925) It has been stated that hydrocortisone has no effect on the blood calcium of patients or animals with functioning parathyroids (*Stoerk et al* 1963) but lowers the blood calcium level in hypoparathyroid patients (*Leifer and Hollander* 1953) and in parathyroidectomized animals of several species (*Mirush and Bosman* 1929 *Stoerk and Arison* 1961) It has also been shown that 3 5 times more parathyroid extract is needed to maintain normal blood calcium concentrations in hydrocortisone injected parathyroidectomized rats than in controls subjected to parathyroidectomy alone The steroid had no effect on the blood calcium of normal animals (*Stoerk et al* 1963) In contrast, it has been reported that an excess of cortisone reduces the normal blood calcium level in young rats (*Laron et al* 1958 *Simmons and Kunin* 1967) This has also been observed in rabbits (*Pincus et al* 1951) *The fall in the blood calcium level* observed in the present study indicates that considerable changes in the calcium metabolism are induced in the adult rat by combined oophorectomy and prednisolone administration After normalization following the significant decrease during the initial 2 and 3 weeks slightly subnormal values were again noted between the 8th and the 14th week of treatment, followed by further normalization

In maintaining the blood calcium at a normal level the bone tissue has an important function as a mineral reservoir (*Copp and Shim* 1963) The results reported by *Stoerk et al* (1963) suggest that stimulated parathyroid function might be involved in the maintenance of the blood calcium level during cortisone administration This would give rise to increased mobilization of skeletal calcium to the blood and these investigators suggest that this mechanism might be responsible for the cortisone induced osteoporosis However in a study of cortisone treated still growing male rats no signs of increased parathyroid activity were observed (*Hansson* 1967) The initial decrease in blood calcium observed in the present study was of such an order of size that stimulated parathyroid function might well have been involved The calcium wasting effect of corticoids is well known (*Gordan et al* 1967) The calcium retaining effect of oestradiol has been demonstrated by *Caldwell* (1962) in growing male rats rendered osteoporotic by combined bilateral adrenalectomy orchidectomy and cortisone treatment Despite continuous cortisone administration oestradiol

DISCUSSION

Corticosteroid administration to young animals always interferes with the normal bone growth (*Follis* 1951, *Sissons and Hadfield* 1955 *Laron et al* 1958 *Kowalewski* 1962, *Stanisavljevic et al* 1962 *Hulth and Olerud* 1963, *Tapp* 1966 *Simmons and Kunin* 1967) When young, still growing animals are used in studies concerning the effects of corticosteroids on the bone mineralization rate the growth inhibitory effect of the treatment must be taken into consideration No such interference could occur in the present study since fully grown, one year old rats were used Only a very slight initial body weight increase occurred in the normal control rats and after 6 weeks of observation the body weight remained unchanged It has been established earlier that in mature female rats no further skeletal growth occurs after a constant body weight has been attained (*Singer et al* 1952) The pronounced decrease in body weight recorded in the experimental animals was caused by depletion of the adipose and muscle tissues due to the treatment In a previous study (*Larsson* 1969 a) the effect on the skeletal tissue was examined in the material used in the present investigation Measurements of the femur length showed no significant differences between normal and corticosteroid treated animals and the epiphyseal zones were closed After the combined treatment with oophorectomy and maintained prednisolone administration for 14 and 16 weeks there was a significant decrease in the ash content of the whole tibia by 6 to 7 per cent which represents a considerable loss of calcium Microradiographs of undecalcified vertebral sections showed that the bone tissue was well mineralized and there was no difference in the degree of mineralization observed on microradiographs from normal and experimental animals It was of interest therefore, to examine the changes in calcium metabolism occurring during the process of bone reduction in these adult rats, especially since earlier work has been confined almost exclusively to the effect of corticosteroids on young growing animals where interference with skeletal growth has to be considered

The significant fall in blood calcium observed in the groups of oophorectomized rats treated with prednisolone for 2 and 3 weeks is of especial interest It has been reported earlier that cortisone administration does not reduce the blood calcium level or affect hypercalcemia induced by vitamin D in young rats (*Williams et al* 1962) In dogs prednisolone treatment results in a significant increase in the blood calcium by 7 per cent (*Garrett et al* 1964) This is in disagreement with observations in humans that in cases of adrenal insufficiency

there is a tendency towards hypercalcemia (*Walser et al* 1963) and that cortisone tends to reverse the hypercalcemia accompanying *different diseases such as* sarcoidosis and hypervitaminosis D (*Dent 1956 Connor et al* 1956) Adrenalectomy further gives rise to increased concentrations of blood calcium in dogs (*Rogoff and Stewart* 1928) rabbits (*Kisch* 1924) and rats (*Rohdenburg and Krehbiel 1925) It has been stated that hydrocortisone* has no effect on the blood calcium of patients or animals with functioning parathyroids (*Stoerk et al* 1963) but lowers the blood calcium level in hypoparathyroid patients (*Leifer and Hollander* 1953) and in parathyroidectomized animals of several species (*Mirvish and Bosman* 1929 *Stoerk and Arison* 1961) It has also been shown that 3 5 times more parathyroid extract is needed to maintain normal blood calcium concentrations in hydrocortisone injected parathyroidectomized rats than in controls subjected to parathyroidectomy alone The steroid had no effect on the blood calcium of normal animals (*Stoerk et al* 1963) In contrast it has been reported that an excess of cortisone reduces the normal blood calcium level in young rats (*Laron et al* 1958 *Simmons and Kunin* 1967) This has also been observed in rabbits (*Pincus et al* 1951) The fall in the blood calcium level observed in the present study indicates that considerable changes in the calcium metabolism are induced in the adult rat by combined oophorectomy and prednisolone administration After normalization following the significant decrease during the initial 2 and 3 weeks slightly subnormal values were again noted between the 8th and the 14th week of treatment, followed by further normalization

In maintaining the blood calcium at a normal level the bone tissue has an important function as a mineral reservoir (*Copp and Shim* 1963) The results reported by *Stoerk et al* (1963) suggest that stimulated parathyroid function might be involved in the maintenance of the blood calcium level during cortisone administration *This would* give rise to increased mobilization of skeletal calcium to the blood and these investigators suggest that this mechanism might be responsible for the cortisone induced osteoporosis However in a study of cortisone treated still growing male rats no signs of increased parathyroid activity were observed (*Hansson* 1967) The initial decrease in blood calcium observed in the present study was of such an order of size that stimulated parathyroid function might well have been involved The calcium wasting effect of corticoids is well known (*Gordan et al* 1967) The calcium retaining effect of oestradiol has *been demonstrated by Caldwell* (1962) in growing male rats rendered osteoporotic by combined bilateral adrenalectomy orchidectomy and cortisone treatment Despite continuous cortisone administration oestradiol

DISCUSSION

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reported by *Clark and Roth* (1961) and to an inhibitory effect of the corticosteroids on normal bone growth resulting in decreased bone mineralization (see below) In dogs prednisolone increases the amount of intravenously administered Ca^{45} eliminated in the faeces and urine (*Collins et al* 1962) and in man cortisone and ACTH increase the calcium excretion in both the urine and faeces (*Luft and Sjogren* 1951) The tubular reabsorption of calcium is reduced in humans treated with corticosteroids possibly due to an anti anabolic effect on the cells of the tubules (*Laake* 1960) The effect of adrenal cortical steroids on intestinal calcium absorption in the rat has been a subject of disagreement According to *Milhaud et al* (1960) corticosteroids decrease calcium absorption However no effect of hydrocortisone on the over all gastro intestinal calcium absorption was found in the rat by *Clark and Smith* (1964)

Administration of hydrocortisone to rats has been reported to inhibit the uptake of Ca^{45} by bone which was also found to be decreased in nephrectomized rats and it was suggested that the limiting factor may lie in the synthesis of chondroitin sulphate (*Clark et al* 1959) Similar conclusions were drawn from the observation that the retention by the rat of injected radioactive strontium and calcium measured over the total body and over the tail was decreased after the administration of dexamethasone (*Bohr and Dawids* 1964) The specific activity of the blood was not determined but because the specific activity of the urine was increased while the urinary output of calcium was normal it was suggested that the decreased retention was due to a reduction in the amount of bone available for mineralization In both these studies interference by the corticosteroids with normal growth might well explain the results obtained especially in the experiment of *Clark et al* (1959) where male rats weighing between 160 and 250 gms were used *Bohr and Dawids* (1964) used female rats weighing about 200 gms and in these animals cortison administration caused a relatively small though definite decrease in the retention of bone seeking isotopes

In the present study the calculated mean accretion rate for the tibia was found to be increased in the groups of oophorectomized animals treated with prednisolone for 1 and 2 weeks while in the groups of rats treated for 3 to 12 weeks approximately normal values were found The groups treated for 14 and 16 weeks showed fluctuating values These experimental results are in agreement with those obtained after administration of various corticoids to normal human volunteers in whom the bone accretion rate did not fall but remained normal or even increased slightly (*Gordan and Eisenberg* 1963) The proposals made by *Clark et al* (1959) and by *Bohr and Dawids* (1964) may be

cured the osteoporotic bone changes in these animals In the rat but not in other species, oestrogens have been reported to inhibit bone resorption (*Budy et al* 1952, *Lindquist et al* 1960) In the present study the significant fall in the blood calcium level was induced by the combination of oophorectomy which resulted in a reduced production of endogenous oestrogens, and daily administration of prednisolone This caused a significant decrease in the mineral content of the whole tibia after treatment for 14 and 16 weeks (*Larsson* 1969 a) The contradictory results obtained in earlier studies concerning the effect of excess corticosteroids on the blood calcium level might be explained by the present findings indicating tha during the progress of the treatment periods of decreased blood calcium values are followed by periods of normal values Furthermore the combination of oophorectomy and prednisolone treatment might have a more pronounced blood calcium lowering effect than corticosteroid treatment alone

The plasma Ca^{45} activity curves indicate an increased elimination rate of intraperitoneally administered Ca^{4} from the blood in the experimental groups in comparison with that of the normal control group On examination of the Ca^{45} activity values of the plasma and the tibia at 72 hours after the isotop injection it is seen that the group of rats treated for 1 week showed decreased plasma Ca^{4} activity and slightly increased Ca^{4} activity in the bone The rats treated for 2 weeks showed approximately normal plasma Ca^{45} activity but slightly increased bone Ca^{45} activity and the group treated for 3 weeks showed approximately the same values for both the plasma and bone Ca^{45} act vity as those of the normal control group The groups of rats treated for 4 to 16 weeks showed concomitant decreases in the plasma and bone Ca^{45} activity values in spite of the fact that with consideration of their body weights these animals were injected with a higher dose of Ca^{45} than the normal controls The Ca^{45} activity of compact bone tissue showed the same decrease as that of the whole tibia although the uptake of Ca^{4} by the compact bone only amounted to less than one fifth of that of the whole tibia These data indicate that prednisolone administration to oophorectomized mature rats results in increased calcium excretion and decreased calcium retention progressing with the duration of prednisolone treatment The decrease observed in the blood calcium level seems to be secondary to poor or retarded adaptation to the increased calcium excretion

It has been reported that corticosteroids increase the excretion of administered bone seeking isotopes in young rats (*Clark et al* 1959 *Milhaud et al* 1960 *Bohr and Dawids* 1964 *Clark and Smith* 1964) In young growing animals this might be due to decreased reabsorption of calcium by the renal tubules as

All the seven groups of rats treated for 4 to 16 weeks showed consistently decreased values for both the plasma and bone Ca^{45} activity

The Ca^{45} activity of compact bone powder was appreciably lower than that of the whole tibia In the three groups of rats treated for 1 2 and 3 weeks the former activity showed approximately the same values as those of the normal control group In the seven groups of rats treated for 4 to 16 weeks consistently decreased values were obtained with a maximum reduction in the groups of animals treated for 12 14 and 16 weeks

The calculated calcium accretion rate for the tibia expressed as mg calcium hour/mg calcium of the tibia showed increased mean values in the groups of rats treated for 1 and 2 weeks compared with that of the normal control group The six groups of oophorectomized rats treated with prednisolone for 3 to 12 weeks showed approximately the same mean values as that of the normal control group In the group treated for 14 weeks a lower mean accretion rate was found while it was higher in the group of animals treated for 16 weeks compared to that of the control group

The presented data show that the hormonal imbalance induced in adult rats by combined treatment with oophorectomy and prolonged prednisolone administration evidently results in increased calcium deprivation because of increased excretion progressing with the duration of prednisolone treatment There was an increased elimination from the blood of intraperitoneally administered Ca^{45} and a corresponding decrease in the uptake of Ca^{45} by bone Except for an initial increase the calcium accretion rate by bone was approximately the same in the experimental and control rats These data indicate indirectly that the significant reduction of bone tissue observed in the same material and reported elsewhere was caused by increased bone resorption which would mobilize skeletal calcium to the blood to normalize the observed significant fall in the blood calcium level

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valid with regard to young still growing animals However in the skeleton of the adult rat in which calcification and growth are completed the accretion rate was normal or even increased after combined oophorectomy and corticosteroid administration This implies that the induced hormonal imbalance did not exert any appreciable inhibitory effect on the bone mineralization rate Evidence was obtained in this investigation to indicate that the decreased skeletal uptake of intraperitoneally administered Ca^{45} is the result of increased elimination of Ca^{45} from the blood due to increased excretion brought about by the treatment The data presented here strongly suggest that the slight reduction of the bone tissue found in a previous study (*Larsson* 1969 a) was caused by increased bone resorption which would mobilize skeletal calcium for maintenance of the blood calcium level With extension of the periods of prednisolone treatment a more pronounced osteoporosis would develop, due to the continuous calcium loss

SUMMARY

Ten groups of 5 fully grown one year old female rats were oophorectomized and then treated with prednisolone for periods varying from 1 up to 16 weeks One control group of 5 normal rats was kept on the same normal laboratory ration for 16 weeks A total loss of body weight by approximately 30 per cent was observed in the group of oophorectomized rats treated with prednisolone for 16 weeks In the normal control rats the body weight showed a slight initial increase but thereafter it remained almost constant throughout the observation period of 16 weeks

The plasma calcium showed a significant fall in the groups of rats treated for 2 and 3 weeks In the group treated for 5 weeks normal values were noted In rats treated for 8 to 14 weeks subnormal plasma calcium values were observed while in the group of rats treated for 16 weeks the values were again normal

There was a higher elimination rate of intraperitoneally administered Ca^{45} from the blood in the experimental groups in comparison with that of the control group The Ca^{45} specific activity of plasma at 72 hours after the isotope injection was significantly decreased in the group of rats treated for 1 week while there was a concomitant tendency to an increase in the Ca^{45} activity of bone In the group of rats treated for 3 weeks the Ca^{45} activity of both plasma and bone showed values similar to those of the normal group

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The Glycosaminoglycans* of Compact Bone Tissue in Experimental Osteoporosis Induced by Prednisolone Treatment of Oophorectomized Rats or by Calcium Restriction**

by

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* The nomenclature of Balazs and Jeanloz (1965) has been followed.

** This work was reported in part at the 15th Scandinavian Congress of Pathology and *Microbiology* Copenhagen June 19—22 1967 see Acta Path. et Microbiol Scandinav suppl 187 61 (1967) and at the Sixth European Symposium on Calcified Tissues August 21—24 1968 see Calc Tiss Res suppl to volume 2 32 (1968)

Abbreviations CPC cetylpyridinium chloride CP cetylpyridinium EDTA disodium ethylenediamine tetraacetic acid

ega dırg the quantitative and qualitative relationships of the glycosaminoglycans in the compact bone tissue of adult rats during the development of two types of experimental osteoporosis induced by (1) oophorectomy combined with prednisolone treatment or (2) prolonged *calcium restriction* The material was analysed mainly by methods based on the solubility properties of the glycosaminoglycan complexes with cetylpyridinium By adapting the technique of *Antonopoulos et al* (1964) information was obtained on the distribution of the chondroitin sulphate with regard to molecular size The isolated chondroitin sulphate was further characterized by physical and chemical methods In addition the concentrations in compact bone tissue of glycosaminoglycans *hexosamines hydroxyproline ash and calcium were* determined in normal conditions and during the development of these two different types of osteoporosis

MATFRIAL

1 Compact bone tissue of normal and prednisolone treated oophorectomized adult rats

Fifty five adult female rats of the Sprague Dawley strain[1] were used All the animals were 11 1/2 to 12 months old at the start of the experiment and had a mean initial body weight of 348 5±2 7 grams The material was divided at random into ten experimental groups and one control group with 5 rats in each. The experimental animals were first oophorectomized via a midline abdominal incision under ether anaesthesia All these animals recovered very quickly after the operation From the third day after the oophorectomy each animal was given 2 5 mg prednisolone[2] daily dissolved in their drinking water, which was supplied intermittently in such a way that the prednisolone was consumed during the following 1—2 hours All animals were housed in individual cages The periods of treatment varied from 1 to 16 *weeks* The control group consisted of 5 normal rats and was observed for 16 weeks The experimental and the control animals received the same ordinary laboratory food ration[3] and tap water All animals *except one survived* through the

[1] Anticimex Co Stockholm

[2] Precortalon Aquosum® Organon kindly supplied by Pharmacia Co Uppsala.

[3] Ewos Co Sodertalje.

INTRODUCTION

Very little is known about the function of the bone glycosaminoglycans. It has been suggested that chondroitin sulphate plays a role in the mineralization stage during bone formation (*Glimcher* 1959, *Sobel et al* 1960) but opinions are divergent.

The formation of glycosaminoglycans of connective tissues appears to be under endocrine control (for ref. see *Brunish* 1966). An inhibitory effect of corticosteroids on the synthesis of glycosaminoglycans in different connective tissues has been demonstrated both *in vitro* and *in vivo*. In view of the decrease observed in S^{35} sulphate incorporation into the chondroitin sulphate of rib cartilage (*Bostrom and Odeblad* 1954, *Whitehouse and Bostrom* 1961) some influence also on bone tissue glycosaminoglycans could be anticipated. However, the effect of excess corticosteroids on the glycosaminoglycans in adult bone tissue does not appear to have been studied. From the finding of a decrease in the ratio of total hexosamine to collagen in the *whole* femur of one year old rats it has been suggested that corticosteroids reduce the content of glycosaminoglycans in bone, which would precede the events leading to the development of osteoporosis (*Sobel and Marmorston* 1954). However these results cannot be interpreted as an effect on bone tissue glycosaminoglycans alone since the articular cartilage of the femur, with its high content of glycosaminoglycans was also included in the specimens. Furthermore the total hexosamine content does not reflect the glycosaminoglycan content alone.

In human osteoporosis, changes in bone matrix have been reported from studies with the aid of X ray diffraction and electron microscopy (*Little et al* 1962). Decreased hydroxyproline contents have been found in bone specimens from the iliac crest in osteoporotic subjects (*Birkenhaeger Frenkel* 1966). With biochemical methods *Casuccio et al* (1962) noted a decrease with age in protein nitrogen and hexosamines, and changes in the glucosamine/galactosamine ratio in several fractions of vertebral bone tissue extracted according to the method of *Dische et al* (1958). The significance of these findings in relation to the osteoporotic process and to a possible role of glycosaminoglycans in this connection is far from clear.

The present investigation was undertaken in order to obtain information

METHODS

Hexosamine was determined by the Elson and Morgan reaction as described by *Antonopoulos et al* (1964) except that a 1 2 scaled down procedure was used in most cases

Aminosugar was characterized by the Dowex 50 H column chromatographic procedure of *Antonopoulos* (1966)

Uronic acid was determined by the carbazol method of *Dische* (1947)

Sulphate was determined by the benzidine method as described by *Antonopoulos* (1962)

Calcium in bone powder was determined by atomic absorption spectrophotometry using a Perkin Elmer Model 303 Instrument About 50 mg of bone powder was ashed at 700 C in a muffle furnace for 16 hours The ash was weighed on a Mettler balance with an accuracy of 0 05 mg and the percentage ash content calculated The ash was then dissolved in 10 ml of 1 2 N hydrochloric acid After dilution to the desired calcium concentration a 5 % lanthanum solution in 25 % (v/v) HCl was added so that the final calcium concentration was within the optimum working range of 1 to 10 ppm and with 0 5 % lanthanum (see Perkin Elmer Rev May 1966) In this way the calcium lanthanum ratio was 1 1000 as recommended by *Willis* (1961) for depression of the phosphorus interference The added calcium recovery in these bone ash solutions was found to be 98 per cent Duplicate determinations were performed throughout The coefficient of variation for these analyses was less than 1 per cent

Hydroxyproline was determined by the method of *Neuman and Logan* (1950) The coefficient of variation for these determinations was 2 per cent

Susceptibility to testicular hyaluronidase[1] was tested by the procedure described by *Solheim* (1965)

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[1] Obtained by the courtesy of Dr B Hogberg AB Leo, Halsingborg Sweden.

period of observation There were no signs of infections or any other intercurrent diseases The experimental animals lost about one third of their initial body weight The femur length was the same as in the normal animals which confirmed that no interference with skeletal growth had occurred

The series was planned so that all the animals were sacrificed at the same time This was performed by bleeding them to death from the femoral artery under ether anaesthesia Immediately after sacrifice the animals were placed in a deep freezer at – 20°C pending the preparations of the long tubular bones The bones were carefully dissected free from soft tissues and periosteum The epiphyses including the cartilage, were removed using a bandsaw The diaphyses were split into small bone fragments which were carefully cleaned from bone marrow with no use of solvents The bone fragments were further defatted and dehydrated with 5 changes of acetone for 3 days The material was finally air dried and then pulverized in an Intermediate model Wiley Laboratory Mill provided with a 60 mesh sieve The defatted dry bone powder obtained was stored in containers with snap caps pending the subsequent analyses

2 Compact bone tissue of normal and calcium deficient adult male rats

Forty one adult male rats of the Sprague Dawley strain[1] were used The experimental animals were 12 to 12 ½ months old at the start of the treatment and were divided into seven groups The control group consisted of five 21 month old rats The mean initial body weight of all rats was 505 2 ± 8 2 grams All animals had been bred on a diet with an optimal intake of calcium phosphorus and vitamin D The experimental animals received a calcium deficient diet[2] containing 0 09 per cent Ca 0 55 per cent P and 2 0 per cent cod liver oil The animals of the experimental groups were supplied with diet and deionized water *ad libitum* for 3 weeks and 6 7 8 9, 10 and 12 months respectively The control group received a normal laboratory ration[3] containing 1 0 per cent Ca and 0 75 per cent P All animals were kept in a sunless room Five deaths occurred among the experimental animals probably related to high age Three of these animals which were frozen immediately after death after 4—6 months on a calcium deficient diet were included in the study however The bones were prepared and the bone powder was produced as described above

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2 Bulletin D 15 General Biochemical Inc Chagrin Falls Ohio USA

3 Ewos Co, Sodertalje

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Amount of hexosamine (expressed as absorbance) in CPC-precipitate per ml of digest various amounts of bone powder were digested. Each point represents the mean of one 2 ml and two 3 ml aliquots from one digest (except the 45 mg digest, where the mean of one 2 ml and one 3 ml aliquot was used)

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weighed on a Mettler balance ...
ash content calculated The
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by *Solheim* (1965)

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Infrared spectrophotometry[1] was carried out using a Unicam SP 200 spectrophotometer The KBr pellet technique was used

Determination of total hexosamine concentration

Hexosamine determination (see above) was performed after hydrolysis of 5 mg bone powder in 1 ml of 6 N HCl for 8 hours After evaporation of the acid, the residue was dissolved in 0 5 ml of water The coefficient of variation was 3 per cent (The residue sometimes contained fine black brown particles Therefore, in some series of determinations 20 mg powder was hydrolysed instead, the residue was dissolved in 2 ml of water and after filtration through a paper[2] the hexosamine was determined on 0 5 ml aliquots The values were the same as when filtration was omitted)

For determination of hexosamine in tissues, *Boas* (1953) recommended an ion exchange step to eliminate non specific chromogens In the case of bone hydrolyzed as described above, this step can be omitted as no such chromogens were found

Determination of the concentration of CPC-precipitable glycosaminoglycans

In a 10 ml volume flask about 45 mg of bone powder was digested at 65°C in about 9 ml of a digestion mixture containing EDTA (pH adjusted to 7 with NaOH) cysteine HCl and recrystallized papain[3] suspension to concentrations of 0 075 M, 0 005 M and 1—2 per cent respectively After 3—6 hours when a clear solution was obtained the volume was brought to the mark with water and the contents thoroughly mixed Three aliquots of 3 0 ml each were pipetted into test tubes 4 ml of a half per cent (w/v) aqueous CPC[4] solution was added to each and the precipitate allowed to settle over night The precipitate was recovered by centrifugation and meticulous decanting and after hydrolysis and evaporation hexosamine determinations were made

Determinations on aliquots from a digest of larger quantity showed a coefficient of variation of 3 per cent

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1 Kindly performed by Dr L Å Fransson Department of Physiological Chemistry University of Lund Lund Sweden

2 Munktell s No OOH S1 80 90

3 Worthington 18 8 mg protein per ml

4 CPC special grade, AB RECIP, Stockholm Sweden

In test experiments, when differen amounts (20 50 mg) of bone powder were d gested it was found that the amount of hexosamine containing material precipitated from 2 or 3 ml of digest was directly proportional to the amount of bone powder digested (Fig 1)

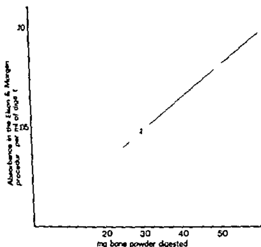


Fig 1
Amount of hexosamine (expressed as absorbance) in CPC-precipitate per ml of digest various amounts of bone powder were digested Each point represents the mean of one 2 ml and two 3 ml aliquots from one digest (except the 45 mg digest, where the mean of one 2 ml and one 3 ml aliquot was used)

Microfractionation of glycosaminoglycans

About 75 mg of bone powder pooled from all animals within each group was digested at 65 C in 50 ml of a digestion mixture containing EDTA cysteine HCl and papain suspension to con entrations of 0 2 M 0 005 M and 1 pro mille respectively for 3—4 hours After dilution with 8 volumes of water o volume of a 1 per cent aqueous solution of CPC was added and the resulting precipitate allowed to settle over night The precipitate was collected by centrifugation in a 100 ml glass tube washed with redistilled water and dried for about half an hour in a desiccator 400 μl of a 60 per cent (v/v) aq eous solution of n propanol was added and the precipitate brought into solution by st rring with a glass rod A fine-disperse residue remained undissolved and was centrifuged down From the clear supernatant 50 μl aliquots were transferred by a constriction pipette to CPC cellulose microcolumns and were fract onated according to the method of *Antonopoulos et al* (1964) with the following eluants 1 p r cent CPC 0 30 M NaCl MgCl solutions with step wise in reasing concentrations from 0 30 to 0 75 M and finally 6 M HCl The salt solutions contained 0 05 per cent CPC.

The fine disperse material, which could not be dissolved in the aqueous propanol was found in test experiments to contain only a few per cent of the whole hexosamine content of the solution When supernatant propanol aliquots were fractionated at the same time as aliquots with undissolved matter stirred up the resulting solubility profiles did not differ noteworthily and recoveries in both cases were about 90 per cent Centrifugation was preferred in the final procedure because of a tendency to clogging in the columns when uncentrifuged solutions were used

Isolation and fractionation of bone glycosaminoglycans on the macroscale

The procedure used by *Hjertquist and Vejlens* (1968) was followed essentially Digestion was performed as described above with 50 ml of digestion mixture per g (3—15) bone powder Eight volumes of water and one volume of a 1 per cent CPC solution were added and after 48 hours the precipitate formed was collected on glass filter paper[1] in a Buchner funnel It was subsequently dissolved in 65 per cent aqueous propanol (The paper was minced in the propanol solution which was then sucked out through a new glass filter until the minced paper was dry) To the clear solution 3 volumes of ethanol were added and the sodium salts of glycosaminoglycans were precipitated by adding a few ml of saturated sodium acetate aqueous solution The precipitated material was recovered by centrifugation and dried with ethanol and ether The powder was dissolved in water and small amounts of undissolved matter were spun down and discarded To the supernatant (3—4 ml) as much of a 2 M NaCl solution was added so as to obtain a final concentration of 0 02 M NaCl after the addition of approximately two volumes of a 1 per cent CPC solution On the following day the precipitated complexes were recovered by centrifugation, washed dried for half an hour in a desiccator and dissolved in 60 per cent propanol A small amount of substance remained undissolved This was suspended and the solution placed on top of a CPC cellulose column, prepared according to *Antonopoulos et al* (1961) Dimensions of columns 1 × 25 cm for 25—40 mg dried polysaccharide 1 × 15 cm for 10 mg Elution was performed with 1 per cent CPC 0 3 M NaCl 0 3 M MgCl and 0 83 M MgCl and finally in some cases 1 0 M MgCl All salt solutions contained 0 05 per cent CPC The collection of fractions detection of peaks (by CP complex precipitation) and

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1 Whatman GF 81

recovery of sodium salts of the glycosaminoglycans were performed as described by *Antonopoulos et al* (1965)

Statistical methods

The analytical data obtained from the rats in each group were subjected to analysis of variance with one way lay out according to *Scheffe* (1961) The hypothesis of no difference between groups was tested at the 5 per cent significance level When a significant result was obtained data of one or more groups were combined in order to find significant contrasts These were tested according to *Scheffe* (1961)

RESULTS

Contents of ash calcium and hydroxyproline

The major components of the defatted dried bone powder i e mineral and collagen were examined by determinations of the ash calcium and hydroxyproline contents In order to reduce the effects of small methodological variations from one occasion to another all samples at each investigation were treated at the same time whenever possible (e g ashing procedure weighing calcium determinations and hydrolysis) otherwise the samples were taken at random for the analyses

In the corticosteroid experiment the ash and calcium contents showed slightly lower values in the three groups of animals treated for 1 to 3 weeks than in the normal control group (Table 1) When the values for these groups combined were tested against those of the normal control group the differences were statistically significant in the case of calcium however only when the groups treated for 2 and 3 weeks were combined In the seven groups of rats treated for 4 to 16 weeks no significant changes were found however The hydroxyproline contents for treated groups showed slightly fluctuating values as compared with those of the control group but the variations were not statistically significant In the calcium deficiency experiment no significant changes were noted in the concentrations of ash calcium or hydroxyproline (Table 2)

Groups		No of animals	Ash %	S F M	Calcium %	S E M	Hydroxy proline ‰	S E M
Normal controls		5	65 51	0 43	25 59	0 38	16 4	0 51
Ooph + prednisolone for	1 week	5	63 21	0 57	24 08	0 28	17 1	0 58
,	2 weeks	5	62 97	0 56	23 56	0 30	17 2	0 32
,	3	5	62 13	0 44	23 54	0 25	16 2	0 44
	4	5	65 57	0 76	24 71	0 37	17 1	0 44
	5	5	66 26	0 56	24 90	0 20	16 1	0 39
	8	5	67 05	0 50	24 73	0 32	16 0	0 35
	10	5	65 60	0 25	24 95	0 24	16 2	0 30
	12	4	65 73	0 15	25 12	0 26	16 2	0 59
	14	5	65 67	0 30	24 88	0 14	17 1	0 22
	16	5	65 61	0 41	25 01	0 24	16 5	0 13
			$F = 10\ 12$ sign		$F = 5\ 34$ sign		$F = 1\ 38$ N S	
					$F_{0\ \%}\ (10\ 43) = 2\ 06$			

Table 1 The concentrations of ash calcium and hydroxyproline in compact bone powder from normal control rats and oophorectomized rats treated with prednisolone for different periods of time (S E M = standard error of the mean)

Groups	No of animals	Ash %	S E M	Calcium %	S E M	Hydroxy proline ‰	S E M
Normal laboratory ration	5	63 13	0 40	24 28	0 23	16 4	0 23
Low cal ium diet for 3 weeks	6	63 48	0 19	23 98	0 30	16 8	0 17
4 6 months	3	63 92	0 39	24 58	0 49	16 1	0 34
6	4	63 37	0 29	24 62	0 20	16 1	0 23
7	4	63 03	0 66	24 39	0 77	16 0	0 28
8	3	6? 55	0 38	23 56	0 25	16 2	0 36
9	5	63 82	0 33	23 88	0 15	16 3	0 37
10	5	63 12	0 26	24 08	0 32	16 4	0 13
12	4	63 71	0 83	24 45	0 77	16 4	0 38
		F = 0 87 N S		Γ = 0 59 N S		Γ = 0 93 N S	
				Γ_{09} (8 30) = 2 27			

Tal le ? The concentrations of ash cal ium and hydroxyproline in compact bone powder from rats fed a *normal* laboratory rati n and rats fed a low cal ium diet for different periods of time

Groups		No of animals	Total hexosamines ‰	S E M	Glycosamino glycans ‰	S E M
Normal controls		5	1 48	0 02	0 39	0 009
Ooph + prednisolone for	1 week	5	1 51	0 01	0 40	0 018
	2 weeks	5	1 56	0 03	0 41	0 015
	3	5	1 49	0 00	0 41	0 023
	4	5	1 46	0 01	0 41	0 012
	5	5	1 49	0 03	0 40	0 017
	8	5	1 46	0 03	0 40	0 015
	10	5	1 41	0 00	0 41	0 020
	12	4	1 46	0 03	0 38	0 007
,	14	5	1 48	0 02	0 40	0 009
,	16	5	1 43	0 01	0 40	0 014
			$F = 3\ 16$ sign		$F = 0\ 49$ N S	
				$F_{0\ 05}\ (10\ 43) = 2\ 07$		

Table 3 The concentrations of total hexosamines and CPC precipitable glycosaminoglycans (as hexosamines) in compact bone powder from normal control rats and oophorectomized rats treated with prednisolone for different periods of time

Groups		No of animals	Total hexosamines ‰	S E M	Gl[illegible]cosamino gl[illegible]cans ‰	S E M
Normal laboratory ration		5	1 55	0 02	0 46	0 008
Low calcium diet for	3 weeks	6	1 48	0 01	0 43	0 006
	4 6 months	3	1 49	0 07	0 44	0 023
	6	4	1 53	0 05	0 46	0 017
	7	4	1 50	0 02	0 4[illegible]	0 017
	8	3	1 49	0 01	0 41	0 026
	9	5	1 53	0 01	0 45	0 012
	10	5	1 55	0 04	0 42	0 018
	12	4	1 48	0 01	0 42	0 024
			F = 0 87 N S		F = 1 20 N S	

$F_{0\ 05}$ (8 30) = 2 [illegible]7

Table 4 The c[illegible]n entrati[illegible]ns of t[illegible]tal hex[illegible]amines and C[illegible]C [illegible]re ipitable glycosamin glycans (as hexosamines) in compact bone powd[illegible]r fr[illegible]m rats fed a normal lab[illegible]ratory rati[illegible]n an[illegible] rat[illegible] fed a l[illegible]w [illegible]al[illegible]ium diet for different perio[illegible] of time

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,	4	5	1 46	0 01	0 41	0 012
	5	5	1 49	0 03	0 40	0 017
	8	5	1 46	0 03	0 40	0 015
	10	5	1 41	0 00	0 41	0 020
	12	4	1 46	0 03	0 38	0 007
	14	5	1 48	0 02	0 40	0 009
	16	5	1 43	0 01	0 40	0 014
			F = 3 16 sign		F = 0 49 N S	

$F_{0\,95}$ (10 43) = 2 07

Table 3 The concentrations of total hexosamines and CPC precipitable glycosaminoglycans (as hexosamines) in compact bone powder from normal control rats and oophorectomized rats treated with prednisolone for different periods of time

The sum of the MgCl fractions (the chondroitin sulphate fraction) constituted about 94 per cent of the eluted hexosamines The means of the values of the $MgCl_2$ fractions from the three columns were used for constructing solubility profiles. In every fractionation experiment two different groups were investigated at the same time and thus tested against each other as shown in Table 5

Table 5 Groups tested pair wise with the microfractionation procedure

ST 10 w ST 3 w	ST 8 w ST 14 w	CaD 6 m CaD 10 m	SC ST 16 w
CaC CaD 12 m	CaD 8 m ST 2 w	CaC ST 2 w	CaC CaD 3 w

w = weeks m = months ST = steroid treatment CaD = calcium deficiency SC = control group steroid experiment CaC = control group calcium deficiency experiment

Two of the groups (ST 2 w CaC) were tested 2 or 3 times against different groups As the two solubility profiles emanating from microfractionations performed simultaneously were always nearly identical it is concluded that there were no differences in the solubility properties of the CP chondroitin sulphate from the different groups When profiles from fractionations performed on different occasions were compared deviations were noted increasing with time and eventually becoming larger than expected on the basis of the reproducibility found previously An increasing parallel shift to the right of the CP-chondroitin sulphate solubility curves was noted Control fractionations showed that this phenomenon was due to a change with time of the solubility properties of the $MgCl_2$ solutions which was not reflected in the titrated Cl^- ion concentrations. This phenomenon might possibly have been caused in some way by the storage of salt solutions in small (10 ml) sealed glass bottles with rubber stoppers (the intention was to minimize evaporation) as such effects have not been seen in other studies when the salt solutions have been stored instead in larger plastic bottles with screw caps

Total hexosamine concentration

The determinations of the total hexosamine concentration were performed on bone powder from the individual rats About twenty 20 mg samples or fifty 5 mg samples of bone powder were weighed and analysed simultaneously In the calcium-deficiency experiment the 5 mg sample analysis was used throughout. Duplicate analyses were performed in approximately one third of the material In the corticosteroid experiment the two groups of rats treated for 1 and 2 weeks showed slightly increased values (Table 3) This increase was not statistically significant however The eight groups of animals treated with prednisolone for 3 to 16 weeks showed no consistent change which could be correlated to the duration of treatment but only a small, insignificant intergroup variation

In the calcium deficiency experiment the values of the eight experimental groups did not differ significantly from those of the control group (Table 4)

Concentration of glycosaminoglycans

The glycosaminoglycan concentration determinations were also performed on bone powder from individual animals Nine samples randomly selected within each of the experimental series were digested and precipitated at the same time Hydrolysis and the remaining steps of the procedure were carried out on 9 or 18 samples simultaneously The results are presented in Tables 3 and 4

No statistically significant differences were found between the various groups within each experimental series No change with the duration of treatment was noted The hexosamines emanating from glycosaminoglycans corresponded to less than a third of the total hexosamines

Microfractionation of bone glycosaminoglycans

In this case 750 mg of pooled bone powder consisting of equal parts from each of the rats in separate experimental and control groups were used Three columns were run for each group The recovery was found to be between 90 and 110 per cent

The fractions eluted with 1 per cent CPC and 6 M HCl only occasionally contained traces of hexosamine

The 0 3 M NaCl fraction constituted about 6 per cent of the sum of the eluted hexosamines and no differences were noted between the control and treated groups

Isolation and characterization of chondroitin sulphate

This was performed on a pool of bone powder from each of the following groups male control group (calcium deficiency experiment) female control group (corticosteroid experiment) calcium deficient groups (from 6 to 12 months on low calcium intake) and prednisolone treated oophorectomized groups (8 to 16 weeks of treatment) The two latter pools comprised 15 g of bone powder each while that of the control group in the calcium deficiency experiment comprised 9 g and in the corticosteroid experiment 3 g The crude isolated glycosaminoglycans amounted to approximately 40 mg from each of the pools of the treated groups and 20 and 10 mg respectively from those of the control groups In every column separation peaks were eluted in the following three salt solutions used 0 3 M NaCl 0 3 M MgCl and 0 83 M MgCl none in 1 % CPC or 1 M MgCl The fractions eluted with 0 3 M NaCl and obtained from the experimental groups in the two series were combined The precipitated material from the corresponding fractions of the control groups was too small for analysis The fractions eluted with 0 3 M MgCl which were recovered from the control groups were combined The amounts isolated as Na salts and the results of chemical and physical characterization of the fractions are given in Table 6 For all the fractions eluted with 0 83 M MgCl the results are in accordance with chondroitin 4 sulphate with a similar degree of sulphation The analytical results of the 0 3 M NaCl fractions and the 0 3 M MgCl fractions are not wholly conclusive It is considered however that the glycosaminoglycans in these fractions constituted a mixture of hyaluronic acid and low molecular and/or low sulphated chondroitin sulphate the former predominating in the NaCl fractions and the latter in the 0 3 M MgCl fractions Corresponding fractions isolated from cortical bone from dogs (*Hjertquist and Vejlens* 1966 1968) have been shown to contain hyaluronic acid and a mixture of hyaluronic acid and chondroitin sulphate respectively

DISCUSSION

Isolation of glycosaminoglycans from tissues by means of papain digestion in the presence of EDTA followed by precipitation of the liberated glycosaminoglycans with cetylpyridinium chloride is now a well established technique As shown by *Hjertquist and Vejlens* (1968) this procedure can also be used for

Table 6 *Chemical and physical characteristics of the various glycosaminoglycan fractions isolated from rat cortical bone*

Fraction	Amount isolated	*Per cent of dry weight* Hexosamine	Hexuronic acid	Sulphate	Hexuronic acid[1] / Hexosamine	Sulphate[1] / Hexosamine	Sulphate / Hexuronic acid	Per cent of hexosamine galactosamine / glucosamine	Susceptibility to hyaluronidase	Infrared pattern in accordance with
0 83 M $MgCl_2$ female controls	3 5 mg	22 5	30 0	14 9	1 23	1 23	1 00	100 / 0	+	Chondroitin 4 *sulphate*
0 83 M $MgCl_2$ *prednisolone* treated	10 0 *mg*	22 7	30 3	15 3	1 23	1 26	1 02	100 / 0	+	Chondroitin 4 sulphate
0 83 M $MgCl_2$ male controls	7 0 mg	18 6	23 6	12 0	1 17	1 20	1 03	100 / 0	+	Chondroitin 4 sulphate
0 83 M $MgCl_2$ Ca deficiency	12 0 mg	*21 8*	29 9	14 4	1 27	1 23	0 97	100 / 0	+	Chondroitin 4 sulphate
0 30 M $MgCl_2$ *female and male controls* pooled	5 0 mg	3	5	not analysed	1 7	—	—	85 / 15	not tested	—
0 30 M $MgCl_2$ prednisolone treated	4 0 mg	7	6		0 9	—	—	70 / 30	"	—
0 30 M $MgCl_2$ Ca deficiency	4 0 mg	4	6		1 5	—	—	75 / 25	,	—
0 3 M NaCl prednisolone and Ca deficiency pooled	4 0 mg	2	2		1 0	—	—	18 / 82	,	—

[1] *Molar* ratios with hexosamine = 1 00
[2] Molar ratios with hexuronic acid = 1 00

bo e provided that the FDTA content of the digestion mixture is high enough to chelate the bone calcium In this latter study chondroitin sulphate amounting to 0 14—0 18 per cent on the basis of total dry weight was isolated from compa t dog bone The amount of chondroitin sulphate isolated from compact rat bone in the present study was only 0 07—0 08 per cent on the same basis These lower values can partly be explained by the higher mineral content of rat bone as compared with dog bone Further a higher percentage loss of chondroitin sulphate during the isolation and purification procedures in the present study is likely because of the smaller amount of initial material available than was used in the investigation by *Hjertquist and Vejlens* (1968)

Other investigations have shown hat chondroitin 4 sulphate is the predominating glycosaminoglycan of compact bone tissue from ox (*Meyer et al* 1956) dog (*Hjertquist and Vejlens* 1968) rabbit and homo (*Vejlens* unpublished) Also in the rat bone studied in the present investigation the main glycosaminoglycan was a sulphated galactosaminoglycan with characteristics of chondroitin 4 sulphate

The original procedure for microfractionation of CP glycosaminoglycans described by *Antonopoulos et al* (1964) was developed on cartilage and allowed a simultaneous quantitative and qualitative analysis Because of the low content of glycosaminoglycans and the high mineral content of the bone tissue examined in the present study quantitative analyses were performed separately from the microfractionation The quantitative determination of the bone glycosaminoglycans as CPC precipitable components of a papain digest is a relatively simple procedure It appears less tedious than the method described by *Bollet* (1958) in which no proteolysis is used protamine is the precipitating agent and dialysis steps are included In the present investigation the amount of bone powder used for the quantitative analyses of the glycosaminoglycans was approximately 50 mg which allowed triple hexosamine determinations from one digest If required a single determination can be performed on only 10—12 mg of bone powder In that case the digestion precipitation and the Elson and Morgan reaction are carried out in the same test tube

Only a minor proportion of the total hexosamines in compact bone tissue originates from acid glycosaminoglycans — in the rat bone analysed in the present study less than a third The major part seems to be associated with glycoproteins (*Herring* 1964 *Burckard et al* 1966)

In the present study the mi rofractionation procedure of *Antonopoulos et al* (1964) was adapted to allow relatively small amounts of bone powder to be analysed for the constru tion of solubility profiles of CP chondroitin sulphate

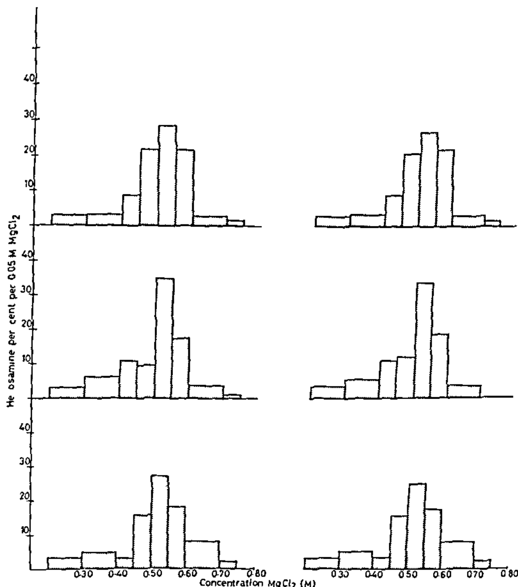


Fig 2 Some representative solubility profiles of the CP chondroitin sulphate Amount of hexosamine expressed as percentage of total hexosamines eluted with $MgCl_2$ solvents Upper profiles left SC right ST 16 w Middle profiles left SC right CaD 12 m Lower profiles left ST 2 w right CaD 8 m (For notation see Table 5) Note the almost identical appearance of solubility profiles on the same horizontal line which are from microfractionations performed in parallel

In previous studies (*Larsson* 1969 c, d) data obtained with the aid of Ca^{45} indicated increased mobilization of skeletal calcium for maintenance of the blood calcium level both after combined oophorectomy and prednisolone administration and after prolonged calcium restriction The results of the present investigation show that during this process of prolonged increased bone resorption the remaining compact bone tissue is quite unchanged with regard to its major components and also to the glycosaminoglycans even after combined oophorectomy and prednisolone treatment for 16 weeks or maintained calcium restriction for up to 1 year Apart from an unchanged concentration there is no change in the molecular weight distribution of the bone chondroitin sulphate as indicated by unchanged solubility profiles at a similar grade of sulphation

The lack of an apparent corticosteroid effect on the glycosaminoglycans of mature bone tissue is further supported by results obtained in a short term study of almost fully mature rabbits treated for 3 weeks with other glucocorticosteroids *i e* dexamethasone 0 5 mg/kg body weight daily or cortisone 3 mg/kg daily The concentrations of total hexosamine glycosaminoglycans hydroxyproline and calcium did not differ from those of control animals and neither did the solubility profiles of the CP complexes of chondroitin sulphate (*Vejlens* unpublished)

These findings suggest that the treatments employed did not cause any changes of the glycosaminoglycans in the bone in any case not in the already formed bone tissue. Although the bone formation rate in old rats is rather low there is some new bone formation which can be observed histologically as a relatively small amount of bone surface showing tetracycline uptake (*Larsson* 1969 a b) The amount of glycosaminoglycans emanating from bone tissue laid down during the shorter periods of treatment may be too small to influence the analytical results Whether this also holds true for longer periods of treatment is more difficult to say However it is not unlikely that the major portion of the glycosaminoglycans of compact bone tissue is synthesized during the period of skeletal growth and that the total turnover of glycosaminoglycans in the normal mature skeleton is very low analogous to that of bone collagen as reported by *Kao et al* (1965) Therefore in the present study an effect of the treatment on glycosaminoglycans of bone tissue during formation cannot be fully excluded especially in the case of steroid administration On the other hand the observed similarities of these two types of osteoporosis may support the possibility of a common more essential factor in the pathogenesis, *e g* enhanced bone resorption because of a need of calcium mobilization. Further studies along these lines particularly concerning the turnover of bone tissue

In order to facilitate the handling of the obtained CP glycosaminoglycan complexes for subsequent solubilization in a small volume of aqueous propanol, somewhat more bone powder (750 mg) was used than was necessary to run three columns Smaller amounts can be used the lower limit for only one column is in the range of 50—100 mg of bone powder

The composition of the bone powder with regard to the relation of mineral/collagen was essentially unchanged in each of the experimental series This supports the view that the rarefaction of the bones observed in previous studies of the same rats (*Larsson* 1969 a b) after longer periods of treatment was, in fact, consistent with osteoporosis The only exception was the slightly lower mineral content per weight of the bone powders from oophorectomized rats treated with prednisolone for 1—3 weeks They did not however exhibit the corresponding increase of hydroxyproline which would be expected if an initial phase of osteomalacia was involved That the lower ash and calcium values mentioned may have originated from a methodological error cannot thus be excluded Furthermore no demineralization of bone tissue was found in rabbits treated with dexamethasone for 3 weeks (*Vejlens* unpublished)

The effect of corticosteroids on the metabolism of glycosaminoglycans has been studied in different tissues both *in vitro* and *in vivo* Using S^{35} labelled sodium sulphate as the tracer substance *Layton* (1951 a b) noted a decrease in the activity of bound sulphate in different tissues after the administration of cortisone The production of glycosaminoglycans by connective tissue cells in tissue culture becomes decreased in the presence of methylprednisolone (*Castor* 1962) Rats given cortisone *in vivo* show a decreased uptake of radioactive labelled sulphate and/or acetate by hyaluronate and chondroitin sulphate isolated from the skin (*Schiller and Dorfman* 1957) The incorporation of S^{3} labelled sodium sulphate in the sulphate groups of chondroitin sulphate of calf cartilage becomes decreased both *in vitro* and *in vivo* (*Bostrom and Odeblad* 1953, *Whitehouse and Bostrom* 1961) In recent years results have been presented suggesting an inhibitory effect of corticosteroids also on the degradation of glycosaminoglycans in rabbit costal cartilage (*Kaplan and Fisher* 1964) Low concentrations of hydrocortisone have no significant inhibitory effect on the synthesis of chondroitin sulphate by cartilaginous embryonic chick tibiotarsi in organ culture but have a marked effect on the distribution of the glycosaminoglycan between the tibiotarsus and the culture medium suggesting inhibited degradation (*Schryver* 1965) As far as the mature bone tissue is concerned nothing has been reported concerning the effect of corticosteroids on the glycosaminoglycans

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SUMMARY

The composition of compact bone from adult rats during the development of experimental osteoporosis was studied Groups of male rats subjected to calcium restriction for various periods up to 12 months and female oophorectomized rats treated with prednisolone for up to 16 weeks were used Adult, normal rats of corresponding sexes served as controls

The dried pulverized bone was analysed for contents of mineral (ash calcium) collagen (hydroxyproline) total hexosamine and glycosaminoglycans (as hexosamine of cetylpyridinium precipitable polysaccharides) The relation of mineral/collagen remained mainly unchanged by the treatments thus confirming that the rarefaction of the bones of animals treated for longer periods noted in previous studies was genuine osteoporosis The concentrations of total hexosamines and of hexosamines originating from glycosaminoglycans were not affected by the treatments Of the latter more than 90 per cent could be accounted for by chondroitin sulphate (see below), and they amounted to less than a third of the total hexosamines

The glycosaminoglycans of the bone tissue both from normal and experimental animals were isolated and fractionated on the macroscale using the cetylpyridinium precipitation method The main component was identified as chondroitin 4 sulphate A smaller part was presumably hyaluronic acid

Smaller amounts of glycosaminoglycans from bone pooled within experimental groups were also isolated as cetylpyridinium complexes applied in propanol solution on microcolumns and fractionated The results indicated that no change in the molecular size pattern of chondroitin sulphate occurred with the different forms of treatment

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GENERAL DISCUSSION

Any attempt to give a survey of the enormous amount of literature concerning clinical osteoporosis meets necessarily with a profusion of contradictory theories of its aetiology (*Dent* 1968) In normal aging there is a gradual steady loss of bone beginning soon after the age of 20 years This has been considered by some authors to be the main cause of human osteoporosis (*Rose* 1967) However there are most likely additional factors accelerating bone loss and giving rise to symptomatic osteoporosis in juvenile adult and also senile patients (*Dent and Watson* 1966) Further investigations regarding such factors are therefore important both from the clinical and theoretical point of view In this respect the reaction of the mature bone tissue to nutritional and hormonal disturbances is of special interest In contrast to the multitude of incoherent data obtained in extensive clinical studies on patients with advanced osteoporosis little information has been provided concerning bone loss in experimental animals Much of the research and interpretation of data has been influenced by the extensive literature on rickets in rats However studies of skeletal growth in young animals do not seem to be relevant to the problems associated with the maintenance of the adult skeleton (*Hegsted* 1967) Also concerning induced hormonal disturbances young animals have been studied almost exclusively Therefore the present investigation was undertaken with the purpose of determining whether or not disturbances induced by a) prolonged calcium restriction and b) oophorectomy combined with prolonged prednisolone administration resulted in changes of the mature bone tissue and calcium metabolism which could be related to the development of osteoporosis according to the definition of *Albright and Reifenstein* (1948)

A Calcium deficiency

Although restricted calcium intake in adult men results in a negative calcium balance persisting for relatively long periods of time (*Malm* 1958) there is no evidence that a reduced calcium intake can in fact give rise to osteoporosis in humans It was stated by *Nordin* (1960) that osteoporosis could be induced in adult animals by low calcium diets However the experimental studies

amounts of vitamin D It was found in accordance with the results reported by *El Maraghi et al* (1965) that a relatively long period of calcium restriction in adult rats does not result in any notable skeletal changes However in the present study an evident reduction of bone mass was observed after 14 to 16 weeks of calcium deficiency These results support those obtained in calcium adaptation studies by *Nicolaysen et al* (1953) and *Henry et al* (1960) that adult rats remain in negative calcium balance for a relatively long period of time after the institution of a low calcium diet The conclusion by *El Maraghi et al* (1965) that a dietary calcium concentration of 0 11 per cent would probably be adequate for maintenance of the calcium balance in old rats therefore appears to be not valid Furthermore it was found in the present investigation that on prolonged calcium restriction there was a successive decrease in the ash content of the whole tibia by 6 2 per cent after 16 weeks and 13.3 per cent after 12 months of calcium deficiency These results are not in agreement with the opinion of *Nicolaysen et al* (1953) that a highly increased efficiency of calcium absorption would compensate for any previous loss in a calcium deprivation period The findings of the present study are more in line with the observations made by the same authors that in adult rats on a moderately calcium deficient diet there is no such compensatory increase of the calcium absorption

Corresponding to the reduction of the ash content of the tibia in the present study there was a decrease in the hydroxyproline content of the metacarpal bone This indicates that there was a concomitant breakdown of minerals and organic bone matrix Further there was a decrease in the density of the humerus Thus a widespread loss of bone mass was observed comprising both cancellous bone recorded as a decrease in the number of vertebral bone hits and compact bone due to endosteal resorption resulting in the observed reduction in cortical bone thickness

Histological examination revealed no signs of osteomalacia or osteitis fibrosa No osteoclasts were observed either in the normal or in the experimental animals In human osteoporosis bone resorption is known to occur without any obvious formation of osteoclasts (*Urist* 1958) Since there is no correlation between the number of osteoclasts and the ability of the bone under parathyroid stimulation to supply calcium to the extracellular fluid (*Talmage* 1967) osteoporosis could possibly develop without any notable formation of osteoclasts The vertebral bone of the osteoporotic animals was evenly mineralized as observed on microradiographs of undecalcified sections and showed no apparent difference from

reported concern almost exclusively young growing animals and have not yielded coherent results

The adult rat is generally considered to be resistent to the development of osteoporosis due to its effective adaptation to a low calcium intake as reported in calcium balance studies (*Nicolaysen* 1960) However, the variability in calcium absorption studies is considerable (*Nicolaysen et al* 1953) and a prolonged slight loss of calcium from the skeleton would be difficult to determine with calcium balance techniques The general principle for the adaptation of calcium absorption to reduced calcium intake in old rats is similar to that in aged humans (*Nicolaysen et al* 1953) The adult rat needs 0 5 per cent calcium in the diet for calcium equilibrium (*Henry and Kon* 1947) and has been reported to remain in negative calcium balance for at least 4 months on restricted calcium intake (*Henry et al* 1960) Therefore the reaction of the skeletal tissue and calcium homeostasis to reduced calcium intake in the adult rat provide special interest with regard to the development of osteoporosis

The effect of instituting a low calcium diet with normal contents of phosphorus and vitamin D on the bone tissue and calcium metabolism has been studied from different points of view in the present investigation on adult rats A short preliminary communication of a part of this study was given by *Larsson and Sevastikoglou* (1966) The studies were planned with the purpose of following the sequence of changes in various parameters which could be related to the development of osteoporosis

It has been suggested from results of calcium balance studies on old rats that a marked adaptation of calcium absorption will occur only when the animals have suffered a substantial loss of calcium from the skeleton This distinctly increased efficiency of calcium absorption would compensate fully for any previous loss (*Nicolaysen et al* 1953) However the results obtained in those studies were not quite conclusive Thus rats fed a low calcium diet *i e* with 0 04 per cent calcium showed a successive increase in calcium absorption while rats given a moderately low calcium diet *i e* 0 25 per cent did not show this reaction even after several months of calcium underfeeding (*Nicolaysen et al* 1953)

In two year old rats fed for 12 weeks with a diet containing only 0 11 per cent calcium and 0 55 per cent phosphorus little if any effect was found in the weight of ash/cm³ in the whole femur (*El Maraghi et al* 1965) In the present investigation adult rats were maintained on an almost similar low calcium diet, *i e* 0 09 per cent calcium and 0 55 per cent phosphorus with adequate

amounts of vitamin D It was found in accordance with the results reported by *El Maraghi et al* (1965) that a relatively long period of calcium restriction in adult rats does not result in any notable skeletal changes However in the present study an evident reduction of bone mass was observed after 14 to 16 weeks of calcium deficiency These results support those obtained in calcium adaptation studies by *Nicolaysen et al* (1953) and *Henry et al* (1960) that adult rats remain in negative calcium balance for a relatively long period of time after the institution of a low calcium diet The conclusion by *El Maraghi et al* (1965) that a dietary calcium concentration of 0 11 per cent would probably be adequate for maintenance of the calcium balance in old rats therefore appears to be not valid Furthermore it was found in the present investigation that on prolonged calcium restriction there was a successive decrease in the ash content of the whole tibia by 6 2 per cent after 16 weeks and 13 3 per cent after 12 months of calcium deficiency These results are not in agreement with the opinion of *Nicolaysen et al* (1953) that a highly increased efficiency of calcium absorption would compensate for any previous loss in a calcium deprivation period The findings of the present study are more in line with the observations made by the same authors that in adult rats on a moderately calcium deficient diet there is no such compensatory increase of the calcium absorption

Corresponding to the reduction of the ash content of the tibia in the present study there was a decrease in the hydroxyproline content of the metacarpal bone This indicates that there was a concomitant breakdown of minerals and organic bone matrix Further there was a decrease in the density of the humerus Thus a widespread loss of bone mass was observed comprising both cancellous bone recorded as a decrease in the number of vertebral bone hits and compact bone due to endosteal resorption resulting in the observed reduction in cortical bone thickness

Histological examination revealed no signs of osteomalacia or osteitis fibrosa No osteoclasts were observed either in the normal or in the experimental animals In human osteoporosis bone resorption is known to occur without any obvious formation of osteoclasts (*Urist* 1958) Since there is no correlation between the number of osteoclasts and the ability of the bone under parathyroid stimulation to supply calcium to the extracellular fluid (*Talmage* 1967) osteoporosis could possibly develop without any notable formation of osteoclasts The vertebral bone of the osteoporotic animals was evenly mineralized as observed on microradiographs of undecalcified sections and showed no apparent difference from

the normal in the amount of bone surface labelled with tetracycline These observations suggest that a slight continuous loss of bone calcium with a concomitant breakdown of organic matrix occurs on the bone surfaces in the adult rat during prolonged calcium restriction This long term process results in osteoporosis

In a unified concept of the pathomechanisms in human osteoporosis the long term process of bone reduction has been related to disturbances in calcium metabolism and the efficiency of calcium homeostasis in maintaining the extra cellular fluid calcium (*Heaney* 1965) Since there are no data demonstrating such a process it was considered of interest to examine the blood calcium level and the distribution of Ca^{45} between blood and bone during the development of the described calcium deficiency osteoporosis

It was found in the present investigation that during the development of calcium deficiency osteoporosis the blood calcium values were slightly subnormal initially and also at later periods of time with normal values in between The hypocalcemia secondary to overfeeding of phosphorus is well known (*Liegeois and Derivaux* 1951) In the present study the dietary phosphorus was normal according to *Henry and Kon* (1947) and the hypocalcemia therefore seems to have been caused by the negative calcium balance induced by the lowered calcium intake The initial transient fall in the blood calcium concentration found in the present investigation corresponds well with that found in short term experiments in healthy adult humans after the institution of a low calcium diet (*Nordin* 1964 *MacFadyen et al* 1965) The hypocalcemia of calcium deprivation in humans is believed to be transient and very small changes in blood calcium concentration are considered to be corrected by bone mineral without the intervention of the parathyroid glands due to the existence of genuine steady state between bone mineral and tissue fluid (*Nordin et al* 1965) During the development of osteoporosis caused by the prolonged negative calcium balance induced in the present investigation slightly subnormal blood calcium values appeared at various periods of time and seemed to be relatively slowly corrected by bone mineral While under normal circumstances the well documented constancy of blood calcium (*Copp et al* 1960) is exquisitely well regulated by means of a negative feedback (*McLean and Urist* 1955) a slightly subnormal blood calcium concentration is seen in prolonged calcium restriction due to the large stresses upon the mechanisms involved in blood calcium regulation This circumstance does not seem to be in line with the proposal made by *Nordin* (1961) that primary depression of ionic calcium as produced

by a low calcium diet would cause undersaturation of tissue fluid and immediate shedding of bone mineral with restoration of the blood calcium level Instead stimulated parathyroid activity might well be involved during the normalization of the blood calcium concentration since a decrease by less than 5 per cent in the blood calcium level may provide an adequate stimulus for in reased production of parathyroid hormone (*Copp* 1963) The possible role played by he pa athy oid glands for the development of the osteoporosis described in the present inve tigation will be the subject of future tudies

The distribution of Ca^{45} between blood and bone at 72 hours after the intraperitoneal administration of the isotope is of special interest with regard to the development of osteoporosis According to *Bauer et al* (1961) 72 hours after the Ca^{45} injection more than 90 per cent of the observed Ca^{45} activity of the bone has b en incorporated into the nonexchangeable fraction of bone salt throu,h accretion The normal distribution of Ca^{45} rapidly changed upon res r ction of the calcium intake in the present tudy After only 1 week of cal ium deficiency there was an increase by approximately 100 per cent in the blood Ca^{45} activity indicating increased calcium retention Since the adaptation of the rat to restricted calcium intake is brought about by increased absorption of calcium (*N colaysen et al* 1953 *Henry et al* 1960) the increased blood Ca^{45} specific activity was due mainly to decreased endogenous Ca^{45} To a minor degree a decrease in urinary Ca^{45} secondary to the observed slight fall in blood calcium might contribute to the increase in the blood Ca^{45} Also in humans adaptation to reduced calcium intake is effected by more efficient absorption (*Malm* 1958 *Thorangkul et al* 1959)

After this initial phase there was an increase by approximately 100 per cent in the deposition of Ca^{45} into bone mineral on the 3rd week of continuous calcium restriction and despite a persistent subnormal blood calcium concentration there was a decrease to the normal level of the blood Ca^{45} specific activity The same distribution of Ca^{45} prevailed also on the 4th and 5th weeks of cal ium restriction The subsequent normalization of the blood calcium concentration after the hypocalcemic period must then have been brought about by increased mobilization of skeletal calcium to the blood The observed increased deposition of Ca^{45} into bone mineral appears to be secondary to the s ill more in reased mobilization of bone calcium.

After the blood calcium concentration had returned to normal on the 5th week of cal um restriction there was another sh ft in the distribution of Ca^{45} between blood and bone Thus on the 8th week of calcium deficiency the Ca^{45}

activity of both blood and bone had reached a level 50 to 60 per cent above that of the normal controls This distribution of Ca^{45} remained unchanged until the 16th week of maintained calcium restriction and during this period the blood calcium was normal

These data clearly demonstra e a persistent increase in calcium retention during prolonged negative calcium balance, induced by continuous calcium restriction In contrast rats fed the test diet enriched with calcium showed significantly decreased Ca^{4} activity of both blood and bone in comparison with the normal controls The results confirm earlier observations (*Hansard et al* 1951 *Nicolaysen et al* 1953 *Carlsson* 1953 *Henry et al* 1960) that animals accustomed to a high calcium intake must adjust their absorptive mechanism to a lowered supply of calcium

With continuation of the restricted calcium intake and the development of osteoporosis slightly subnormal blood calcium values were again observed in rats kept on the low calcium diet for 16 weeks and 6 and 7 months Subsequently between 8 to 12 months of calcium restriction the blood calcium was normal During the hypocalcemic period another shift in the Ca^{45} distribution indicated that a new dynamic balance was induced in these animals by the prolonged calcium deficiency Thus, the blood Ca^{4} specific activity showed an increase by 100 to 200 per cent while the Ca^{45} activity of bone was increased by only about 40 per cent In these animals the contribution of structural changes in cancellous bone to the balance and distribution of calcium must be considered Due to the loss of cancellous bone and of cortical bone from the endosteal surfaces the amount of bone surface available for intense calcium deposition *i e* surface accretion is reduced There was no apparent change in the amount of fluorescent bone surface as observed with the tetracycline labelling method These circumstances would therefore contribute to the highly increased blood Ca^{45} specific activity observed in these osteoporotic animals Further acceleration of calcium absorption as suggested by *Nicolaysen et al* (1953) and *Henry et al* (1960) would have a similar effect

This dynamic sequence of events found in the present investigation demonstrates that with a negative calcium balance induced by prolonged calcium restriction the efficiency of calcium homeostasis in maintaining extracellular fluid calcium is the primary pathomechanism for the development of this type of osteoporosis During the loss of bone mineral there are shifts in the calcium dynamic balance at different periods of time associated with the occurrence of a slightly subnormal blood calcium concentration

In clinical osteoporosis the bone accretion rate or mineralization rate is usually reported to be normal (*Heaney and Whedon* 1958 *Fraser et al* 1960 *Dow and Stanbury* 1960 *Dymling* 1964 *Nordin et al* 1964) However both a decreased accretion rate (*Bauer et al* 1957 *Eisenberg and Gordan* 1961 *Lafferty et al* 1964) and an increased (*Nordin* 1959) have also been found It was therefore considered of interest to estimate the accretion rate in the normal and osteoporotic animals of the present investigation In 4 groups of rats fed the low calcium diet for 7 8 9 and 10 months the estimated mean accretion rate values for the *whole* tibia (mg calcium/hour/mg calcium of the tibia) were similar to that of the normal control group In 2 groups of rats fed the low calcium diet for 6 and 12 months respectively lower values were obtained as compared with that of the control group These data are in agreement with those reported in human osteoporosis A normal accretion rate was also reported by *Copp and Suiker* (1962) for 4 month old rats fed a low *calcium diet i e 0 037* per cent calcium and *0 43 per cent phosphorus* for 6 months In this latter experiment the effect of the treatment on the skeletal tissue was not studied further When the calcium accretion rate by bone in osteoporotic individuals is compared with that in normals differences in bone mass must be considered Furthermore in the present study the higher Ca^{45} activity of bone marrow blood of the osteoporotic animals compared with that of the normal controls also has some influence on the values obtained These circumstances make it difficult to draw any conclusions regarding the calcium accretion rate by the bone tissue *per se* The data obtained in the present study only suggest that there is no appreciable difference from the normal in the retention of calcium by the *whole* tibia and probably by the *whole* skeleton of the osteoporotic rats It is pointed out that calcium accretion by bone cannot be equated with bone formation since the amount of tracer localized as diffuse uptake in the bone tissue is too high and variable to allow such a correlation (*Rowland* 1960)

Lactating female rats have been reported to develop osteoporosis on feeding with a low calcium diet (*Tomlin et al* 1953 *McClendon and Blaustein* 1965) Those changes could be reversed by the administration of tricalcium phosphate (*McClendon and Blaustein* 1965) However the morphological criteria of *osteoporosis used i e basophilia of the bone* trabeculae fibrosis and increased clasmatocytic activity suggest that the bone lesions induced might have been osteitis fibrosa rather than osteoporosis Kittens fed a low calcium high phosphorus diet develop osteitis fibrosa (Greaves et al 1958) This condition is also well known in young cats kept on a low calcium high phosphorus meat

diet (*Scott* 1957, 1959, *Roberts and Scott* 1961) and has been shown to be caused by nutritional secondary hyperparathyroidism (*Krook et al* 1963) While young cats develop osteitis fibrosa, adult cats fed a similar low calcium, high phosphorus meat diet *i e* 0 007 per cent calcium and 0 18 per cent phosphorus on a wet weight basis have been reported to develop osteoporosis (*Jowsey and Gershon Cohen* 1964) In these adult cats there was an increased bone resorption accompanied by an increase in number of newly formed osteones Contrary to the experience in clinical osteoporosis the reduction in bone mass was reversed by feeding a high calcium diet In that experiment and in an extended similar study (*Jowsey and Raisz* 1968) the induced bone changes were related to observed secondary hyperparathyroidism However, in the latter experiment cats fed the low calcium meat diet for 5 months showed a definite osteomalacia while cats maintained on this diet for 13 months were reported to have developed osteoporosis since the osteoid borders, although highly increased in frequency, were of normal width The decrease in bone resorption but not in formation observed in such osteoporotic animals after treatment with a high calcium diet for 1 month suggested that the bone changes induced by the low calcium diet could be reversed This condition differs from that in human osteoporosis by the markedly increased bone formation, osteoporosis in man being characterized by an increase in resorption alone with the bone formation remaining relatively normal Furthermore young dogs receiving a low calcium diet develop skeletal changes typical of osteitis fibrosa (*Campbell and Douglas* 1965) as also do mature dogs maintained on a low calcium high phosphorus diet (*Saville and Krook* 1968) Horses fed either a low calcium high phosphorus diet (*Krook and Lowe* 1964) or optimal calcium but excessive amounts of phosphorus (*Gries* 1966) develop osteitis fibrosa due to nutritional secondary hyperparathyroidism This condition has also been reported in swine fed diets unbalanced in calcium and phosphorus (*Brown et al* 1966) According to *Jowsey* (1968), growing animals fed a diet low in calcium and high in phosphorus easily develop a frank secondary hyperparathyroidism with depressed serum phosphate and eventually depressed serum calcium osteitis fibrosa and a gross hyperplasia of the parathyroids while in the adult animals the same calcium deficient diet produces no biochemical changes of this kind but symptoms similar to osteoporosis These findings do not seem to be in accordance with results reported for mature dogs fed a low calcium high phosphorus diet (*Saville and Krook* 1968) In these animals there was a decrease in gross bone density and histological examination of decalcified bone sections showed the presence of numerous osteoclasts with the appearance of resorption cavities and further osteoblasts

and osteoid tissue covering the surfaces of cancellous bone Despite the definitely increased amount of osteoid tissue the calcium accretion rate by bone was normal This might suggest qualitative changes in the bone tissue due to the observed secondary hyperparathyroidism The opinion has been held that excessive parathyroid hormone prevents the mineralization of osteoid since the glucoproteins do not undergo depolymerization which necessarily must precede mineralization (*Krook et al* 1963) On the other hand it has been proposed *that the parathyroid hormone caused depolymerization of the ground substance in bone* (*Engel* 1952 *Engel et al* 1953) *Further in* an elevated bone *resorption* as in secondary hyperparathyroidism osteolysis *i e* osteocytic resorption of cells surrounded by matrix containing acid glycosaminoglycans is considered to play an important role (*Belanger* 1965)

In the processes of calcification and decalcification the protein polysaccharides are probably of importance as controlling factors since at the concentration in which they are found in the vicinity of calcifying sites they would certainly affect the distribution and movement of calcium and phosphate in those regions The present concepts of the role of the ground substance in calcification has been discussed in a recent extensive review (*Bowness* 1968) Arguments were presented that acid glycosaminoglycans of ground substance possess properties and occur in situations which would enable them to exert an influence on both the rate and the extent of calcification and decalcification With regard to human osteoporosis it is of interest that fractions of bone glycosaminoglycans extracted according to *Dische et al* (1958) have been reported to be influenced by both aging and osteoporosis A versene soluble component, rich in galactosamine was reduced 50 per cent and the galactosamine/glucosamine ratio was decreased in aged or osteoporotic subjects (*Cassucio et al* 1962) *Since* these changes have been related to the osteoporotic *process it was considered* of interest to examine the glycosaminoglycans of compact bone tissue during the development of calcium deficiency osteoporosis in the present investigation From the findings described above changes in the ground substance of bone *could be expected in a condition of protracted increased* bone resorption No experimental studies appear to have been reported previously concerning the relationship of the bone glycosaminoglycans to such a long term *process* of bone reduction Preliminary reports of this work have been presented by *Larsson and Veilens* (1967 1968)

In normal animals and in animals examined at different stages of calcium deficiency in the present study no changes were found in the contents of ash,

calcium or hydroxyproline of the compact bone tissue Further, there were no changes in the concentrations of total hexosamines and acid glycosaminoglycans In acutely increased bone resorption induced by administration of parathyroid extract, the mobilization of bone calcium has been related to metabolic changes in organic bone matrix (for references see *McLean* 1956 *Geschwind* 1961) No such changes were found during the long term bone reduction in the present investigation From the finding of a decrease in bone matrix hexosamine in rats treated with parathyroid extract for varying periods of up to 3 days it has been suggested that the dissolution of organic bone matrix and calcium mobilization are closely correlated effects of parathyroid hormone (*Johnston et al* 1961) However, in dogs treated for 3, 4 or 5 days with parathyroid extract no changes have been found in either the concentrations of hexosamines and glycosaminoglycans of the compact bone tissue or the molecular weight distribution of the chondroitin sulphate (*Hjertquist and Vejlens* 1968) Administration of parathyroid hormone for 3 days to guinea pigs has been reported to cause a significant decrease in the concentration of calcium but no change in concentration of hydroxyproline DNA or uronic acid of the compact bone A small but not significant decrease in the bone hexosamine concentration occurred (*Bollet et al* 1963) It was suggested that mobilization of mineral from bone occurs without a concomitant decrease in the concentration of matrix constituents The discrepancies of the results might be due to various factors such as differences in species age of the animals periods of treatment and doses of administered parathyroid extract During the prolonged process of bone reduction resulting in calcium deficiency osteoporosis in the present investigation there were no changes in the concentrations of minerals collagen (determined as hydroxyproline) hexosamines or glycosaminoglycans of the compact bone tissue

It was found in the present investigation that in the compact bone tissue of the adult rat the hexosamines corresponding to acid glycosaminoglycans constituted approximately one third of the total hexosamine concentration The main component of the acid glycosaminoglycans was found to be chondroitin 4 sulphate which was shown by *Meyer et al* (1956) to be the predominating glycosaminoglycan of bovine compact bone tissue Apart from an unchanged concentration of the bone chondroitin sulphate there was no change with the development of osteoporosis in its molecular weight distribution as indicated by recorded unchanged solubility profiles and grade of sulphation This indicates that there was no depolymerization of the glycosaminoglycans of the compact bone tissue during the development of osteoporosis induced by prolonged calcium restriction

It is concluded that prolonged calcium restriction in adult rats results in a slight continuous loss of bone calcium due to the efficiency of calcium homeostasis in maintaining the blood calcium concentration at the expense of the bone mass From histological microradiographic and tetracycline labelling studies and biochemical analysis of the remaining compact bone tissue evidence was obtained indicating that the bone changes induced do in fact correspond to osteoporosis according to the definition of *Albright and Reifenstein* (1948)

B Combined oophorectomy and prednisolone administration

The role of corticosteroid hormones in the homeostasis of the adult skeleton is not clear in contradistinction to their well documented inhibitory effect upon normal skeletal growth and development Although it has been pointed out in a review by *Silberberg and Silberberg* in 1956 that adult animals should be used in studies of the relationship between steroid hormones and osteoporosis most available data are still derived from experiments on young animals The interference of the administered hormones with normal bone growth makes it difficult to make any inferences from such experiments with regard to the maintenance of the mature skeleton and the development of osteoporosis in the adult individual The osteoporotic bone changes reported in young growing rats after treatment with corticosteroids for various periods of time (*Kahn and Skoryna* 1959 *Storey* 1960 *Borberg and Lucker* 1964) and in young rats first subjected to bilateral adrenalectomy and orchidectomy (*Caldwell* 1962) seem to be related to the anti anabolic effect of corticosteroids upon the normal development of the skeleton Anabolic hormones were found to prevent the osteoporosis reported by *Borberg and Lucker* (1964) and oestrogens cured the osteoporosis reported by *Caldwell (1962)* despite continuous cortisone administration This curative effect might also be due to the fact that in young rats oestrogens inhibit bone resorption (*Budy et al* 1952 *Lindquist* 1960) Young mice also have been reported to develop osteoporotic bone changes upon cortisone treatment and these can also be prevented with oestrogens (*Glickman and Shklar* 1955)

It is well known that corticosteroids induce cytologic changes in the young growing skeleton while in the mature bone this effect is less evident In young rabbits there is a reduction in number of osteoblasts and new bone formation due to diminished cell division while osteoclast formation and bone resorption continue (*Hadfield* 1955 *Storey* 1957 *deValderrama and Vunuera* 1965) This effect on the bone cell populations results in a massive resorption of

calcium or hydroxyproline of the compact bone tissue Further there were no changes in the concentrations of total hexosamines and acid glycosaminoglycans In acutely increased bone resorption induced by administration of parathyroid extract, the mobilization of bone calcium has been related to metabolic changes in organic bone matrix (for references see *McLean* 1956 *Geschwind* 1961) No such changes were found during the long term bone reduction in the present investigation From the finding of a decrease in bone matrix hexosamine in rats treated with parathyroid extract for varying periods of up to 3 days it has been suggested that the dissolution of organic bone matrix and calcium mobilization are closely correlated effects of parathyroid hormone (*Johnston et al* 1961) However in dogs treated for 3, 4 or 5 days with parathyroid extract no changes have been found in either the concentrations of hexosamines and glycosaminoglycans of the compact bone tissue or the molecular weight distribution of the chondroitin sulphate (*Hjertquist and Vejlens* 1968) Administration of parathyroid hormone for 3 days to guinea pigs has been reported to cause a significant decrease in the concentration of calcium but no change in concentration of hydroxyproline DNA or uronic acid of the compact bone A small but not significant decrease in the bone hexosamine concentration occurred (*Bollet et al* 1963) It was suggested that mobilization of mineral from bone occurs without a concomitant decrease in the concentration of matrix constituents The discrepancies of the results might be due to various factors such as differences in species age of the animals periods of treatment and doses of administered parathyroid extract During the prolonged process of bone reduction resulting in calcium deficiency osteoporosis in the present investigation there were no changes in the concentrations of minerals, collagen (determined as hydroxyproline) hexosamines or glycosaminoglycans of the compact bone tissue

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bone in young rabbits while old animals respond only to a slight degree (*Storey* 1961) Studies in young rats have provided evidence suggesting that in this species the cellular response to excess corticosteroids is dependent also on calcium intake and the ratio of calcium to phosphorus in the diet Thus when the diet contains high, balanced amounts of calcium and phosphorus, cortisone administration results in dense metaphyseal bone due to inhibition of both the formation and resorption processes (*Follis* 1951 *Storey* 1960) With a normal decreased or unbalanced Ca/P intake the response of the metaphyseal bone is the same as in rabbits (*Sissons and Hadfield* 1956 *Storey* 1960 *Simmons and Kunin* 1967)

Since bone actively participates in homeostatic processes in the body the well recognized effect of adrenal cortical hormones upon calcium metabolism might also influence the bone tissue In young growing animals the inhibitory effect of corticosteroids on growth makes it difficult to evaluate the hormonal influence on calcium metabolism and bone mineralization *per se* In a recent study on young rats the calcium metabolism was studied with the aid of Ca^{45} and the growth rate was determined by repeated labellings with tetracycline It was found that during treatment with corticosteroids the calcium accretion rate showed a reduction corresponding to the inhibition of growth (*Bohr* 1968)

It is evident from the findings discussed above that the maturity and age of the skeletal tissue are of decisive importance for the effect exerted by excess corticosteroid hormones In the present investigation one year old rats which had passed the period of active growth were used Histological examination of vertebral bone of the control rats revealed morphological changes which could be attributed to normal chronologic or physiologic aging Morphological changes due to physiologic aging of bone have been described in aged humans (*Sherman and Selakovitch* 1957) and are considered to be more pronounced in patients with severe osteoporosis (*Urist et al* 1963) In the present study the morphological appearance of the bone tissue was similar in the prednisolone treated oophorectomized rats and the normal controls In the vertebral bone tissue no osteoclasts at all were observed either in the normal controls or in the oophorectomized rats treated with prednisolone for varying periods up to 16 weeks A small amount of bone surface showing tetracycline uptake was the only sign of low osteoblastic activity Despite the time interval of 10 days between the two administered doses, only a narrow fluorescent line was seen in the normal rats A similar low degree of tetracycline labelling was also observed in the oophorectomized prednisolone treated rats

In the present study there was a significant decrease by 6 to 7 per cent in the ash content of the whole tibia after treatment with oophorectomy combined with administration of prednisolone for 14 or 16 weeks There was a slight but insignificant decrease in the hydroxyproline content of the whole metacarpal bone, the gross bone density of the humerus and the percentage of vertebral bone hits On direct measurement, a significant reduction was observed in the corti al thickness of the mid shaft of the femur probably caused by increased endosteal bone resorption On microradiographs of undecalcified vertebral sections the bone tissue was evenly mineralized in both normal and experimental animals These findings suggest that in adult rats combined treatment with oophorectomy and prednisolone administration for prolonged periods of time i e at least 14 or 16 weeks results in moderate osteoporosis

Being a part of the connective tissue bone is also affected by the influence of steroid hormones on the formation and development of this tissue The greater effect observed in young growing rats in the experiment by *Caldwell* (1962) might be due to the well known anti anabolic action of cortisone on collagen synthesis as reported by *Smith and Allison* (1965) while in the present study this interference would probably be rather small since bone collagen in rats is synthesized predominantly at an early age (*Kao et al* 1965) Besides an inhibitory effect on the synthesis of bone collagen a direct degrading effect upon bone collagen similar to that on dermal collagen as reported by *Houck and Patel* (1965) and *Kowalewski* (1966) must be considered However there are other reports suggesting only an anti anabolic action of corticosteroids on collagen synthesis but no effect on the catabolism of collagen (*Ki irikko et al* 1965 *Smith and Allison* 1965) The metabolism of bone collagen in relation to the development of experimental osteoporosis will be a subject of future study

In view of the above discussion it is of interest that the significant decrease n ash content of the whole tibia in the groups of oophorectomized rats treated with prednisolone for 14 or 16 weeks corresponds to that previously observed in male rats after specific calcium restriction for the same periods of time Thus in the former the decrease amounted to 6 1 per cent and in the latter to 6 2 per cent This suggests that changes in calcium metabolism induced by this hormonal disturbance might be of special interest with regard to the development of this type of osteoporosis In this respect the effe t on the blood calcium level the distribution of intraperitoneally administered Ca⁴ between blood and bone and on the calcium accretion by bone would provide further

information A study of these effects has been reported in part previously (*Larsson* 1968)

It was found in the present investigation that combined treatment with oophorectomy and prednisolone administration resulted in a slight initial fall in the blood calcium concentration followed by a return to normal values corresponding to the observations after the institution of a low calcium diet in adult male rats Thus, with both these different disturbances slightly subnormal blood calcium values were noted in groups of rats treated for 1 2 3 and 4 weeks Also at later periods of time slightly subnormal blood calcium values were recorded While no effect of cortisone on the blood calcium level was found in young rats by *Williams et al* (1962) and an increase was observed after prednisolone administration to dogs (*Garrett et al* 1964), there are other reports indicating that cortisone lowers the blood calcium in young rats (*Laron et al* 1958 *Simmons and Kunin* 1967) and in rabbits (*Pincus et al* 1951) These contradictory results might be due to such factors as the age of the experimental animals the calcium intake and duration and the dose of corticosteroid hormone administered From the observation that hydrocortisone reduces the blood calcium in patients with hypoparathyroidism (*Leifer and Hollander* 1953) and in parathyroidectomized animals of different species (*Mirvish and Bosman* 1929 *Stoerk and Arison* 1961) it has been suggested that failure to observe the same effect in normal animals was due to secondary hyperparathyroidism (*Stoerk et al* 1963) From the findings in young rats that the hypocalcemia following parathyroidectomy is aggravated by hydrocortisone and that 3 5 times more parathyroid extract is needed to sustain normal blood calcium concentrations in the presence of hydrocortisone it has been suggested that the development of cortisone osteoporosis might be due to secondary hyperparathyroidism and increased bone resorption (*Stoerk et al* 1963) However in a recent study of cortisone treated young rats a slight decrease in blood calcium was recorded but there were no morphological signs of increased parathyroid activity (*Hansson* 1967) Since the animals were fed a high calcium diet it is possible that this prevented the development of secondary hyperparathyroidism A recent preliminary study of the parathyroids in cortisone treated adult rabbits give no conclusive results as to the effect of cortisone alone or cortisone plus excess calcium (*Adams and Jowsey* 1967) Thus, the role played by the parathyroids in the development of cortisone osteoporosis remains to be determined The effect of the hormonal disturbance induced by combined oophorectomy and prolonged prednisolone administration on the parathyroid function will be a subject of future study

In the present study there was an increased elimination from the blood of intraperitoneally administered Ca^{45} after oophorectomy combined with prednisolone administration for varying periods of time Furthermore a change from the normal was observed in the distribution of Ca^{45} between blood and bone examined 72 hours after isotope injection After an initial phase combined treatment with oophorectomy and prednisolone administration for 4 to 16 weeks resulted in a concomitant decrease in the Ca^{45} activity of blood and bone These findings indicate that in the adult rat the hormonal disturbance induced by combined oophorectomy and prolonged prednisolone administration results in an increased loss of calcium persisting throughout the period of treatment The slight decrease observed in the blood calcium concentration seems to be secondary to poor or retarded adaptation to this calcium wasting effect

Corticosteroid administration has been reported to increase the excretion of injected bone seeking isotopes in young rats (*Clark et al* 1959 *Milhaud et al* 1960 *Bohr and Dauids* 1964 *Clark and Smith* 1964) In young growing animals this might be due to decreased reabsorption of calcium by the renal tubules as reported by *Clark and Roth* (1961) but also to an inhibitory effect of the corticosteroids on normal bone growth resulting in decreased bone mineralization as demonstrated by *Bohr* (1968) The reports regarding the effect of corticosteroids on intestinal calcium absorption in the rat are not fully conclusive Thus a decreased calcium absorption was reported by *Milhaud et al* (1960) while no effect on the over all gastro intestinal calcium absorption was found by *Clark and Smith* (1964) In dogs prednisolone increases the amount of intravenously administered Ca^{45} eliminated in the faeces and urine (*Collins et al* 1962) and in humans cortisone and ACTH increase the calcium excretion in both faeces and urine (*Luft and Sjogren* 1951) The reabsorption of calcium by the renal tubules has been reported to be reduced in humans treated with corticosteroids possibly due to an anti anabolic effect of the hormone on the tubular cells (*Laake* 1960)

In young growing rats excess corticosteroids have been reported to inhibit the uptake of bone seeking isotopes by bone (*Clark et al* 1959 *Bohr and Dauids* 1964) and it has been suggested that the limiting factor may lie in the synthesis of chondroitin sulphate (*Clark et al* 1959) In the adult fully grown rats used in the present investigation the estimated mean calcium accretion rate for the tibia was found to be increased in the two groups of oophorectomized rats treated with prednisolone for 1 and 2 weeks while in six groups of animals treated for 3 to 12 weeks approximately normal values were found Two groups of rats treated for 14 and 16 weeks showed fluctuating values These results

information A study of these effects has been reported in part previously (*Larsson 1968*)

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aging and more abruptly with osteoporosis (*Cassucio et al* 1962) The significance of these findings in relation to the osteoporotic process remains to be determined As reported previously in the present investigation neither quantitative nor qualitative changes of the bone glycosaminoglycans were found during the development of calcium deficiency osteoporosis In view of the hormonal influence on the metabolism of glycosaminoglycans in other connective tissues (*Dziewiatkowski* 1964 *Priest* 1967) hormonal disturbances could be expected to influence also the glycosaminoglycans of the bone tissue However no reports appear to have been made previously regarding the effect of excess corticosteroids on the glycosaminoglycans of mature bone tissue

As already mentioned there was a significant decrease in the ash content of the tibia in rats treated by oophorectomy combined with prednisolone administration for 14 or 16 weeks On chemical analyses no significant changes in the concentrations of ash calcium or hydroxyproline in the compact bone tissue were found in these animals These findings indicate that the loss of minerals from the whole bone corresponds to osteoporosis Furthermore no changes were found in the concentrations of hexosamines or acid glycosaminoglycans in the compact bone tissue The main glycosaminoglycan was a sulphated galactosaminoglycan with infrared characteristics compatible with chondroitin 4 sulphate In previous experiments corticosteroids have been reported to decrease the concentration of hexosamines in other connective tissues without reducing the collagen content (*Sobel et al* 1958) However the suggestion of *Sobel and Marmorston* (1954) that a decrease in bone glycosaminoglycans might precede the events which lead to the development of osteoporosis in Cushing s disease seems to be refuted by the results obtained in the present investigation With regard to the metabolism of acid glycosaminoglycans in other connective tissues there is now good evidence that the turnover of the acid glycosaminoglycans and their corresponding polysaccharide protein complexes is fairly rapid at least in comparison with the turnover of collagen (*Bostrom* 1968) The turnover rate of glycosaminoglycans is related to the age of the individual and varies in different tissues In the adult rat the biological half life of chondroitin sulphate in skin has been estimated to be 8 to 11 days (*Bostrom and Gardell* 1953 *Schiller et al* 1956) and in cartilage 16 days (*Bostrom and Gardell* 1953) The incorporation of S^{35} into the glycosaminoglycan fraction of shaft bones of rats of different ages has been studied by *Takemitsu* (1961) In rats 7 days old the specific activity of the radioactive sulphur in the glycosaminoglycan fraction reached a peak 18 hours after the intraperitoneal administration of $Na_2S^{35}O_4$ and the half life time was 6 7 days In older animals there was

indicate that in the adult rat the hormonal disturbance induced by combined oophorectomy and prolonged prednisolone administration causes no apparent decrease in the bone mineralization rate The findings by *Clark et al* (1959) and *Bohr and Dawids* (1964) are in line with the observation that in growing rats excess corticosteroids reduce the calcium accretion rate in correspondence with the inhibition of growth (*Bohr* 1968) The results of the present study are in agreement with those reported in adult healthy humans (*Gordan and Eisenberg* 1963) and in humans treated with corticosteroids (*Nordin et al* 1963 *Nordin et al* 1964) Normal or even increased bone accretion has been reported in osteoporotic patients treated with corticosteroids and it has been suggested that the eventual decrease in bone mass caused by excess corticosteroids might be the result of accelerated bone resorption (*Eisenberg* 1966) The calcium wasting effect of combined oophorectomy and prednisolone administration in adult rats demonstrated in the present investigation indicates that the considerable loss of bone mineral observed after treatment for 14 or 16 weeks was brought about by increased bone resorption which would mobilize bone calcium for maintenance of the blood calcium concentration With extension of the periods of prednisolone treatment a more pronounced osteoporosis would develop due to the continuous calcium wasting

On histological examination of the vertebral bone in the present study areas showing basophilic staining with haematoxylin eosin were observed in the metaphyseal bone trabeculae In sections stained with azocarmine G these areas exhibited only light or no staining and were found to be located in spaces intervening between parallel fibered bone The evident metachromasia with toluidine blue at pH 4 4 indicated that these areas of intercellular substance probably consisted of acid glycosaminoglycans extending into the trabecular bone as remnants from the epiphyseal cartilage according to *Dziewiatkowski et al* (1957) and *Campo and Tourtellotte* (1967) There was no change in metachromasia after the combined treatment with oophorectomy and prednisolone administration From the findings in cortisone treated one year old rats of a decrease in the hexosamine content of the whole femur but no change in the collagen content it has been suggested that a decrease of glycosaminoglycans precedes the events leading to the development of osteoporosis in Cushing s disease (*Sobel and Marmorston* 1954) However this observation may be unspecific with regard to the glycosaminoglycans of the bone tissue itself and no support for this theory is obtained from the findings of the present study

Changes in bone glycosaminoglycans in fractions of vertebral bone tissue extracted according to *Dische et al* (1958) have been reported in normal human

GENERAL SUMMARY AND CONCLUDING REMARKS

1 The aim of the investigation was to determine in the adult rat whether or not disturbances induced experimentally by a) prolonged calcium restriction and b) oophorectomy combined with prolonged prednisolone administration resulted in changes of the mature bone tissue and calcium metabolism which could be related to the development of osteoporosis according to the definition of *Albright and Reifenstein* (1948) Further the studies were planned with the purpose of following the sequence of changes in various parameters which could be related to the development of the disorder An attempt was made to investigate the possible relationship of changed bone mass to alterations in calcium metabolism under these two conditions Further the possible effect of these different disturbances on the compact bone tissue was studied with special regard to the glycosaminoglycans

2 Introductory remarks are made on certain aspects of clinical osteoporosis with special reference to the pathogenesis

3 A critical survey is made of the literature concerning experimental osteoporosis induced by calcium deficiency or corticosteroid administration

4 The effect of prolonged calcium restriction on the skeletal tissue was studied in adult male rats The ash content of the tibia showed values decreasing significantly with time After 16 weeks there was a decrease by 6 2 per cent and after 12 months by 13 3 per cent indicating a continuous slight loss of bone minerals throughout the experimental period The hydroxyproline content of the metacarpal bone showed also a significant decrease indicating a concomitant breakdown of organic bone matrix Radiographic examination showed reduced cortical thickness of the tubular bones and decreased density of the trabecular pattern in the metaphyseal bone after calcium restriction for 6 months and longer These animals showed significantly lower values for the femur score and the vertebral bone hits than the normal controls No change in mineralization of the vertebral bone was observed on examination

a gradual shift until the peak was reached at 48 hours the specific activity of sulphur decreased, and the half life time became shorter Although the metabolic turnover of the bone glycosaminoglycans *in toto* probably decreases with increasing age the combined treatment with oophorectomy and prednisolone administration for varying periods up to 16 weeks could be expected to have some effect on the formation of the bone glycosaminoglycans in the old rats used in the present study After corticosteroid treatment a decrease in incorporation of S^{35} sulphate into chondroitin sulphate of bovine cartilage *in vitro* has been reported (*Bostrom and Odeblad* 1954 *Whitehouse and Bostrom* 1961) However a possible inhibitory effect on the bone glycosaminoglycans might have been too small to influence the analytical quantitative results obtained in the present investigation On the other hand diminution of both the formation and breakdown of the chondroitin sulphate caused by the excess corticosteroids as reported by *Schiller and Dorfman* (1957) in a study on rat skin, is also possible From the findings of an increase of hyaluronate in the vitreous humor and an increase of keraton sulphate in costal cartilage of rabbits treated with prednisolone it has been suggested that corticosteroids have an overall inhibitory effect on the degradation of these glycosaminoglycans (*Kaplan and Fisher* 1964) A similar effect has also been reported in a study on the synthesis of chondroitin sulphate by cartilaginous embryonic chick tibiotarsi in organ culture (*Schryver* 1965)

Apart from an unchanged concentration there was no alteration in the molecular weight distribution of the bone chondroitin sulphate as indicated by unchanged solubility profiles and sulphation grade, after combined treatment with oophorectomy and prednisolone administration in the present study This indicates that there was no depolymerization of the glycosaminoglycans of the compact bone tissue during the development of the osteoporosis induced by this hormonal disturbance

To summarize in the adult rat both prolonged calcium restriction and hormonal disturbance induced by combined oophorectomy and prolonged prednisolone administration lead to a significant reduction of the skeletal tissue fulfilling the criteria of osteoporosis given by *Albright and Reifenstein* (1948) During this prolonged process of increased bone resorption changes in calcium metabolism and the efficiency of calcium homeostasis in maintaining extracellular fluid calcium appear to constitute the primary pathomechanism for the development of the disorder Neither quantitative nor qualitative changes were found in the glycosaminoglycans of the remaining compact bone tissue during this long term process of increased bone resorption

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6 The composition of compact bone from adult rats during the development of calcium deficiency osteoporosis was studied The glycosaminoglycans were analysed using the cetylpyridinium precipitation method No significant changes were recorded in the concentrations of ash calcium hydroxyproline total hexosamines or hexosamines originating from the glycosaminoglycans The unchanged relation of mineral/collagen confirmed that the induced bone rarefaction was genuine osteoporosis according to the definition of *Albright and Reifenstein* (1948) The main glycosaminoglycan was chondroitin 4 sulphate and a smaller part presumably hyaluronic acid The unchanged solubility properties of the chondroitin sulphate—cetylpyridinium complexes and unchanged sulphation grade indicated that no change in the molecular size pattern of chondroitin sulphate occurred during the development of the osteoporosis Of the hexosamines originating from glycosaminoglycans more than 90 per cent could be accounted for by chondroitin sulphate and they amounted to less than a third of the total hexosamines

7 The effect of combined oophorectomy and prolonged prednisolone administration on the skeletal tissue was studied in adult rats The excess of corticosteroids caused considerable depletion of adipose and muscle tissues and significant atrophy of the adrenal cortex (zona fasciculata) During the observation period of 16 weeks no radiographic signs of osteoporosis were seen A significant reduction by 6 1 per cent in the ash content of the tibia was recorded after 14 and 16 weeks of treatment The "femur score showed significantly decreased values while there was only a slight though not significant decrease in the percentage of vertebral bone hits the hydroxyproline content of metacarpal bone and the density of the humerus Microradiographic examination of undecalcified vertebral bone sections showed no changes in degree of mineralization Only a small amount of bone surface showing tetracycline labelling was observed both in normal and experimental animals Histological examination of decalcified sections of vertebral bone from normal and experimental animals showed morphological changes which could be attributed to physiologic aging of bone In the metaphyseal bone of the vertebrae areas were observed which stained metachromatically with toluidine blue at pH 4 4 No change in metachromasia was observed in oophorectomized rats treated with prednisolone for different periods of time

8 The effect of combined oophorectomy and prolonged prednisolone administration on the blood calcium level and the distribution of Ca^{45} between

of microradiographs of undecalcified sections Tetracycline fluorescent micro graphs showed no difference from the normal These findings indicate that the rarefaction of bone represented osteoporosis No osteoclasts were observed in normal or experimental rats In the metaphyseal bone, areas were observed which were metachromatic with toluidine blue at pH 4 4 No change in metachromasia was observed in osteoporotic animals Rats fed the test diet enriched with calcium for 16 weeks showed a tendency to increased ash content, decreased hydroxyproline content and increased density of whole bones compared with normal controls which might suggest a possible increase in degree of calcification

5 The effect of prolonged calcium restriction on the blood calcium level and the distribution of Ca^{45} between blood and bone was studied in adult male rats The blood calcium was slightly subnormal 1 to 4 weeks after commencement of calcium restriction The blood Ca^{45} specific activity 72 hours after the isotope injection showed an increase by 100 per cent after 1 week of calcium restriction, indicating increased calcium retention Animals treated for 3 or 4 weeks showed similar values to the normal controls but increased deposition of Ca^{45} into the skeleton by 100 per cent despite subnormal blood calcium On the 8th to 14th week of calcium deficiency normal blood calcium values and increased Ca^{4} activity in blood and bone by 50 to 60 per cent were recorded indicating continued increase in the retention of calcium Rats treated for 4 to 7 months showed subnormal blood calcium while in animals fed the diet for 8 to 12 months normal values were found Osteoporotic animals kept on the low calcium diet for 6 to 12 months showed highly increased blood Ca^{4} activity by approximately 200 per cent while the uptake of Ca^{45} by bone was increased by 40 per cent In animals fed the diet enriched with calcium the blood Ca^{45} activity was 40 per cent and bone Ca^{45} activity 60 per cent lower than in controls indicating decreased retention of calcium The mean calcium accretion rate for the tibia (mg calcium/hour/mg calcium of the tibia) was decreased in rats fed the low calcium diet for 6 and 12 months while rats treated for 7 8 9 and 10 months showed approximately the same values as the control group From the Ca^{45} data obtained it was deduced that the maintenance of the blood calcium level was brought about by increased mobilization of skeletal calcium to the blood During the loss of bone minerals there were shifts in the calcium dynamic balance at different periods of time associated with the occurrence of a slightly subnormal blood calcium concen tration

to that observed after pure calcium restriction for the same periods of time The calcium wasting effect of this hormonal disturbance observed with the aid of Ca* and the mainly unchanged calcium accretion rate by the bone indicate that the loss of bone minerals was *due to increased bone resorption This seems* to be the essential factor in the pathogenesis of this type of osteoporosis which is further supported by the absence of quantitative or qualitative changes in the bone glycosaminoglycans

II The essential features of the investigation are summarized in the general discussion The results are discussed in relation to reported contradictory result of animal experiments The importance of calcium homeostasis in the pathogenesis of osteoporosis is pointed out

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BO J LUNDBERG

THE FROZEN SHOULDER

CLINICAL AND RADIOGRAPHICAL OBSERVATIONS
THE EFFECT OF MANIPULATION UNDER GENERAL ANESTHESIA.
STRUCTURE AND GLYCOSAMINOGLYCAN CONTENT OF THE JOINT CAPSULE.
LOCAL BONE METABOLISM.

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I INTRODUCTION

A THE FROZEN SHOULDER

DUPLAY in 1872 de cribed a condition peri arthrite scapulo humérale , which differed from arthritis in its symptoms and clinical course

He also suggested manipulation of the shoulder joint under general anaesthe ia as a treatment for the restricted mobility in this disorder

The true nature of this condition has been discussed ever since DUPLAY himself believed that a subacromeal bursitis was the basic cause of the pain and dysfunction However already KLAPP (1916) and RIEDEL (1916) believed that the joint capsule was affected and in con equence PAYR (1931) tried to accompli h a distension of the retracted capsular tissue by intraarticular injections

CODMAN (1934) pointed out that stiffne s and pain in the shoulder could occur without noticeable exogenous influences and he separated this condition from the heterogenous group referred to as periarthritis of the shoulder He termed the condition frozen shoulder" an expression which later has been generally accepted and used synonymously with humero scapular periarthritis in a restricted en_e

CODMAN was of the opinion that the frozen houlder was cau ed by tendinitis in the short rotators Several investigators have related the condition to changes in various periarticular structures (BOSWORTH 1940 LIPPMANN 1943 MOSELEY 1945 DEPALMA 1952 MCLAUGHLIN 1961, LIDSTROM 1963)

However other investigators (NEVIASER 1945 YOUNG and PEARSON 1952 QUIGLEY 1956 HARMON 1958 DE SÈZE et al 1960 1961) favoured the opinion that the joint cap ule was the site of the basic pathological changes in frozen shoulders

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Attempts have been made to relate the disease to various circumstances such as inactivity, strain and pre existing shoulder affection The importance of the latter was studied by PASILA (1965) Examining cases of periarthritis of the shoulder, "tendinitis" without restricted mobility, he did not find that this condition during the course of the disease developed into frozen shoulder

The therapy of *frozen shoulders* has been based on the varying opinions of the basic cause of the disease It is rather difficult to draw any final conclusions from the literature One reason is the indistinct definitions The lump diagnosis "periarthritis" has been used in a wide as well as in a limited sense and this has greatly contributed to the confusion It seems important to restrict the diagnosis of frozen shoulders to cases with a distinct limitation of mobility in the humero scapular joint It is also necessary to separate cases with known exogenous causes or pre existing injuries from cases without or with a doubtful history of exogenous influence

B PURPOSE

The purpose of the present investigation was to collect further information from a series of individuals suffering from the frozen shoulder syndrome Except for clinical observations of these cases the following methods were applied

1 Manipulation under general anaesthesia
2 Arthrography
3 Measurements of the joint volume
4 Surgical exposure
5 Histological examination
6 Chemical analysis
7 In vivo bone densitometry
8 Mineral tracer studies

The emphasis in the study has been on the examination and presentation of clinical variables

Comment

Payr (1931) noticed a reflux when he injected periarthritic joints The volume in normal shoulder joints has been estimated to 16—35 cc (Harmon 1958 De Sèze 1961 and Reeves 1966) It has previously been stated that the joint capacity is reduced in F S (Nelson 1952 Harmon 1958) De Seze et al (1916) found volumes as small as 5—6 cc in F S Vialla et al (1964) found higher intraarticular pressures for a given injected volume in F S as compared to normal joints Both variables pressure and volume reflect the same condition capsular retraction

In the present study it has been demonstrated that the volume of the joint is related to the severity of the disease The finding suggests volumetry as a complimentary diagnostic test of capsular retraction

VII OPERATIVE FINDINGS

Twenty shoulders were exposed surgically through an anterior incision before the manipulation, 15 were Primary and 5 Secondary F S In 6 shoulders the subscapular tendon was dislocated and the capsule incised In these cases the incision considerably released the humero scapular mobility The manipulation was then completed in the usual way After the brisement, the joint surface of the head of the humerus could be felt through the ruptured capsule

In conjunction with the surgical exposure of these joints the following observations were made

a) Periarticular inflammatory changes, especially in the insertion of the rotator cuff on the greater tubercle

b) Thickening of the joint capsule

c) No intraarticular adhesions

d) No signs of rupture of the subscapular tendon during the manipulation

The surgical exposure also provided material for the chemical analysis and the histological examinations described later

VIII HISTOLOGICAL EXAMINATION OF THE JOINT CAPSULE

A LIGHT MICROSCOPY

From 14 F S 12 Primary and 2 Secondary, in which the shoulder was exposed surgically biopsies were taken from the lower anterior portion of the joint capsule The samples were embedded in paraffin sectioned and stained with haematoxylin eosin, with toluidine and according to VAN GIESON

Samples were also collected from the same part of the shoulder joint in individuals with a normal range of motion who were operated on for various reasons mostly habitual dislocation of the shoulder

In the reference cases S S and D A (Table V) the biopsies were taken within a month after traumatic lesions, which however were not associated with a decreased range of motion (rotator cuff rupture and traumatic shoulder dislocation respectively)

The samples were studied with respect to thickening and vascularity of the synovial lining and denseness vascularity and hyperplasia of the adjacent fibrous layer The morphological ranking of the sections was done by a pathologist who did not know their origin[1]

The results of the histological study are shown in Table V In general, the connective tissue in the reference shoulders was organized in bundles or groups of bundles with comparatively few fibrocytes In sections from joint capsules of F S the fibrous tissue appeared more compact or dense (referred to as denseness in the Table) In addition to the impression of denseness there were more cells mostly fibroblasts and sometimes increased vascularity (Appendix A) The synovial lining was largely unchanged except for the fact that in F S capillaries were observed more often No difference between F S and normal could be demonstrated in the metachromatic staining of the toluidine treated sections

The general impression of the morphological changes in the joint capsule in F S was that of *fibrosis and fibroplasia*

COMMENT

It was not possible to collect reference cases of the appropriate age and sex distribution There is however no evidence that changes of the type found in the F.S reflect age and sex only

[1] J G Norden, M D., Department of Pathology General Hospital Malmo

NEVIASER (1945) found signs of chronic inflammation and fibrosis in the sub synovial layers of F S, "capsulitis" DEPALMA (1952) found histological evidence of a low grade chronic inflammatory process not only in the fibrous joint capsule but also in various periarticular structures

The present study supports these findings but no significant amount of inflammatory cells was found The morphology was similar to that of DUPUYTREN'S contracture (NORDEN 1969) ASK UPMARK (1944) stated that

Table V *Histological findings in sections of shoulder joint capsules*

0 no changes
1 slight changes
2 obvious changes
3 extensive changes
— missing in the section

Case	Sex	Age	Synovial lining		Fibrous layer		
			Thickening	Vascularity	Denseness	Fibroplasia	Vascularity
References							
M N	M	19	0	0	0	0	0
A C	M	22	0	0	0	0	0
K O	M	22	0	0	0	0	0
M P	M	25	0	0	0	0	0
H R	M	26	—	—	0	0	0
S A	M	35	0	0	0	0	0
K R	M	44	0	0	0	0	0
G J	M	52	—	—	0	0	0
S S	M	63	1	0	0	1	2
I M J	F	25	0	0	0	0	0
D A	F	75	2	2	1	1	2
Frozen shoulders							
E R	M	55	0	0	2	2	2
S B	M	64	0	2	2	2	0
G K	F	42	—	—	1	1	0
E B N	F	45	—	—	1	0	0
G A	F	45	1	1	2	2	0
E S	F	47	0	0	2	2	0
E H	F	50	0	2	2	2	0
I P	F	51	0	2	2	3	2
J P	F	52	0	0	2	0	0
E M	F	53	0	2	2	3	2
M M	F	55	—	—	1	0	0
H N	F	64	0	0	2	3	0
P W[1]	F	51	—	—	2	2	0
T S[1]	F	55	0	0	0	0	2

[1] Secondary frozen shoulders

such palmar infilt ations were common in cardiosclerotic patients with *shoulder disorders* DUPUYTREN'S contracture was present in 25 % of SCHAER'S (1936) cases of periarthritis of the shoulder KLAMI (1962), however could *not demonstrate* any such relationship

B ELECTRON MICROSCOPY

In order to obtain information concerning the individual fibrils including their periodicity the *ultrastructure of the joint capsule was studied in samples from 4 normal shoulders and 3 Primary F S*

The samples were prefixed in 2 5 % glutaraldehyde in phosphate buffer pH 7 2 fixed in 1—2 % osmium tetroxide (MILLON c 1962) and embedded in Vestopal W Sections were made with an *LKB* microthome Ultrotome and examined in a *Hitachi HS 7S electron* microscope Some sections were stained in lead citrate (REYNOLDS 1963) [1]

The sections were studied and photographed with special reference to the appearance and arrangement of the collagen bundles and individual fibrils The general impression in F S was that of a more compact arrangement of the collagen fibres there were also as was expected from light micro copy more cellular elements present Between normal shoulders and F S there was no indication of differences in structure or periodicity of the fibrils (Appendix A) The variation of collagen appearance was not greater between pathological and normal sections than between sections from the same shoulder

COMMENT

The character of the capsular changes in the F S leads to the suspicion that the properties of collagen in the tissue are changed, and that the F.S is a symptom of disease in the collagen itself Electron micro copy of capsules from a limited number of shoulders did not indicate structural changes

[1] The preparation was supervised and the photographs examined by C. v. Mecklenburg Fil. D Department of Zoology University of Lund Lund

NEVIASER (1945) found signs of chronic inflammation and fibrosis in the sub synovial layers of F S, "capsulitis" DEPALMA (1952) found histological evidence of a low grade chronic inflammatory process not only in the fibrous joint capsule but also in various periarticular structures

The present study supports these findings but no significant amount of inflammatory cells was found The morphology was similar to that of DUPUYTREN'S contracture (NORDEN 1969) ASK UPMARK (1944) stated that

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2 obvious changes
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Case	Sex	Age	Synovial lining		Fibrous layer		
			Thickening	Vascularity	Denseness	Fibroplasia	Vascularity
References							
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A C	M	22	0	0	0	0	0
K O	M	22	0	0	0	0	0
M P	M	25	0	0	0	0	0
H R	M	26	—	—	0	0	0
S A	M	35	0	0	0	0	0
K R	M	44	0	0	0	0	0
G J	M	52	—	—	0	0	0
S S	M	63	1	0	0	1	2
I M J	F	25	0	0	0	0	0
D A	F	75	2	2	1	1	2
Frozen shoulders							
E R	M	55	0	0	2	2	2
S B	M	64	0	2	2	2	0
G K	F	42	—	—	1	1	0
E B N	F	45	—	—	1	0	0
G A	F	45	1	1	2	2	0
E S	F	47	0	0	2	2	0
E H	F	50	0	2	2	2	0
I P	F	51	0	2	2	3	2
J P	F	52	0	0	2	0	0
E M	F	53	0	2	2	3	2
M M	F	55	—	—	1	0	0
H N	F	64	0	0	2	3	0
P W [1]	F	51	—	—	2	2	0
T S [1]	F	55	0	0	0	0	2

[1] Secondary frozen shoulders

T ble VI *Hexosamine f om FCTLOLA (I) and CPC-microcellulose column (II III) fractionation as percentage of total in dry defatted synovial tissue f om shoulder j ints with unlimited and restricted mobility In III the tissue glycosaminoglycans have been precipitated by CPC prior to fractionation. Stepwise elution with 1 ml of each of the solutions (Average ± S E)*

	Fract n	I				II						III					
		H₂O and 0 02 M HCl	0 5 M NaCl	6 M HCl	Total ug/mg dry tissue wt	1 % CPC	0 3 M NaCl	0 3 M (neutral) MgCl	0 75 M (acid) MgCl	6 M HCl	Total ug/mg dry tissue wt	1 % CPC	0 3 M NaCl	0 3 M (acid) $MgCl_2$	0 7 M (acid) $MgCl_2$	6 M HCl	Total ug/mg dry tissue wt
References	Average	64 2	15 9	"0 .	8 0	71 8	15 7	1 6	2 0	9 0	7 3	10 9	40 9	. 5	5 1	41 3	1 6
	S E	. 17	0 82	1 73	0 39	1 44	0 91	0 80	0 76	1 16	0 44	2 70	3 39	1 13	2 17	3 81	0 19
	N	13				13						12					
Frozen Shoulders	Average	54 0	16 7	"9 6	9 9	67 4	12 6	6 0	5 0	9 0	8 76	7 1	20 9	7 0	13 4	51 9	2 14
	S E	2 05	1 09	1 89	0 5	2 35	1 .8	1 24	0 60	1 6.	0 55	1 14	1 46	2 98	1 57	4 03	0 16
	N	1.				14						8					
	P (t te t of difference)	<0 01	—	<0 001	<0 01	—	—	<0 01	<0 01	—	<0 0.	—	<0 001	—	<0 01	—	<0 05

IX ANALYSIS OF GLYCOSAMINOGLYCANS[1] IN THE JOINT CAPSULE

A MATERIAL

From 14 surgically exposed F S, two of which were secondary, biopsy specimens were taken from the joint capsule for chemical analysis (LUNDBERG 1969) Similarly biopsies were taken from 13 cases with a free range of motion, who were operated on, mostly because of habitual shoulder dislocation Differences in age and sex distribution between the two groups existed to the same extent as in the histological study and for the same reasons

B CHEMICAL ANALYSIS [2]

The glycosaminoglycans were liberated from the capsular tissue by papain digestion according to SCOTT (1960)

The glycoproteins were separated from the glycosaminoglycans by chromatography of 50 μl of the digestion mixture (corresponding to about 2 5 mg dry weight of the capsule) on ECTEOLA columns as described by RINGERTZ and REICHARD (1960) By this procedure the glycoproteins were recovered after elution with water and 0 02 M HCl, the unsulfated glycosaminoglycans with 0 5 M NaCl and the sulfated with 6 M HCl (Table VI 1)

For further determination of the glycosaminoglycans they were precipitated as water insoluble cetylpyridinium complexes on columns of powdered cellulose and fractionated as described by ANTONOPOULOS et al (1964) by washing with salt solutions of increasing concentrations (Table VI 2) To each micro cellulose column was added 50 μl of a digest equivalent to approximately 2 5 mg dry capsule

Larger amounts of material, corresponding to approximately 25 mg of dry tissue weight, were fractionated on cetylpyridinium chloride (CPC) cellulose microcolumns according to THUNELL's (1967) modification With this method the glycosaminoglycans were precipitated with 1 % aqueous CPC and fractionated before and after treatment with testicular hyaluronidase (Table VI 3)

[1] Equivalent to mucopolysaccharides according to the terminology of BALAZS and JEANLOZ (1965)

[2] The work was carried out under supervision of S Gardell M D at the Department of Physiological Chemistry University of Lund Lund

T ble VI Hexosamine f om ECTEOLA (I) and CPC-microcellulose column (II III) fractionat on as percentage of total in dry d fatted synovial tissue from shoulder joints with unlimited and restricted mobility In III the tissue glycosaminoglycans have been precipitated by CPC prior to fractionation Stepwise elution with 1 ml of each of the solutions (Average ± S E)

		I				II						III					
	Fraction	H₂O and 0 02 M HCl	0 5 M NaCl	6 M HCl	Total ug/mg dry tissue wt	1 % CPC	0 3 M NaCl	0 3 M (neutral) MgCl	0 75 M (acid) MgCl	6 M HCl	Total ug/mg dry tissue wt	1 % CPC	0 3 M NaCl	0 3 M (acid) MgCl₂	0 7 M (acid) MgCl₂	6 M HCl	Total ug/mg dry tissue wt
References	Average	61 2	15 9	40 2	8 0	71 8	15 7	1 6	2 0	9 0	7 3	10 9	40 9	2 5	5 1	41 3	1 6
	S E	2 17	0 82	1 73	0 39	1 44	0 91	0 80	0 76	1 16	0 44	2 70	3 39	1 13	2 17	3 81	0 19
	N	13				13						12					
Frozen Shoulders	Average	54 0	16 7	29 6	9 9	67 4	12 6	6 0	5 0	9 0	8 76	7 1	20 9	7 0	13 4	51 9	2 14
	S E	2 05	1 09	1 89	0 52	2 35	1 28	1 24	0 60	1 62	0 55	1 14	1 46	2 98	1 57	4 03	0 16
	N	12				14						8					
	P (t te t of difference)	<0 01	—	<0 001	<0 01	—	—	<0 01	<0 01	—	<0 05	—	<0 001	—	<0 01	—	<0 05

C RESULTS

The available amount of material was too small to permit an identification of the glycosaminoglycans in the synovial tissue from shoulder joints However, on the basis of results obtained from studies on the glycosaminoglycans in human knee joint capsules (HEINEGARD et al 1968) it was possible to determine the origin of the hexosamines in the present study

The results presented in Table VI imply, regardless of method, an increased total amount of hexosamines in the synovial tissue of the F S as compared to normal The increase was confined to the sulfated glycosaminoglycans There was a significant reduction of the glycoprotein content in the F S joint capsule as evaluated from the decreased amount of hexosamine recovered after elution with water and 0 02 M HCl of the digested material on ECTEOLA columns The hyaluronic acid exclusively present in the 0 3 M NaCl fraction (HEINEGARD et al 1968) was also reduced (Table VI 3) Concerning the sulfated glycosaminoglycans the same study indicated that the 0 3 $MgCl_2$ fraction corresponded to heparan sulfate while the chondroitin 6 sulfate and the dermatan sulfate were recovered in the subsequent fractions

The values of the latter fractions were higher in samples from the F S There were no differences in the degree of dermatan sulfate hybridization between frozen and normal shoulders as indicated by the effect of hyaluronidase treatment (FRANSSON and RODEN 1967) This analysis revealed that dermatan sulfate is a major component of the glycosaminoglycans in joint capsules

COMMENT

Some parallels may be drawn between the composition of granulation tissue and synovial tissue of F S SYLVEN (1941) found metachromasia in regenerating tissue of healing wounds VINOGRADOV (1966) demonstrated that an increase of glycosaminoglycans was associated with intense proliferation of fibroblasts Hyperplasia of the fibroblasts and an increase of the glycosaminoglycans are characteristic for the joint capsules of F S BERENSEN and DALFERES (1960) found that the content of chondroitin sulfate in granulation tissue increased more rapidly than that of hyaluronic acid in the present study those components were changed in the same direction It may be suggested that the changes in the glycosaminoglycans are characteristic for a repair reaction AKESON et al (1967) found in experimentally immobilized knees of dogs a decrease of the contents of hyaluronic acid and chondroitin sulfate in the periarticular connective tissue Therefore the findings in the present study may reflect not a secondary effect of immobilization but rather the pathogenesis of the condition

V LOCAL CHANGES IN BONE METABOLISM

A BONE DENSITOMETRY

1 Material and Methods

In 40 cases of Primary F.S 23 women and 17 men the bone mineral mass of the head of the humerus was evaluated In addition 10 men and 10 women randomly selected among persons *without any history of injury to the upper limb*, were measured The method which has been described in detail elsewhere (NILSSON 1966 LUNDBERG and NILSSON 1968) made use of the radiation from a source of Americium 241 The attenuation of a photon beam from the source was measured as the beam passed through the head of the humerus the soft tissue was accounted for by the use of a water phantom of the same thickness as the bone and soft tissue interposed in the path way of the beam

All individuals included in this study were right handed There was no preponderance for left or right in this group of Primary F S Their average age is given in figure 12

2 Results

In the reference cases the head of the left humerus contained less mineral expressed as the thickness in the path way of the beam (g/cm²) than did the right This difference was however significant only in women

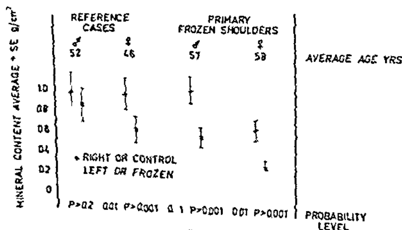


Fig 12
The mineral content of the head of the humerus

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X LOCAL CHANGES IN BONE METABOLISM

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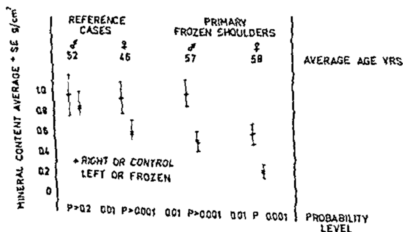


Fig 12

The mineral content of the head of the humerus

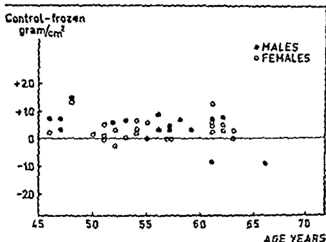


Fig 13
Degree of osteopenia in primary frozen shoulders as a function of age

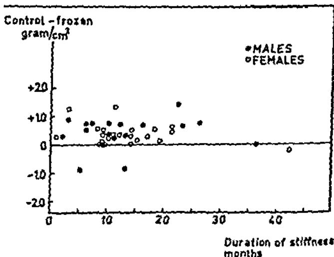


Fig 14
Degree of osteopenia in primary frozen shoulders as a function of the duration of stiffness

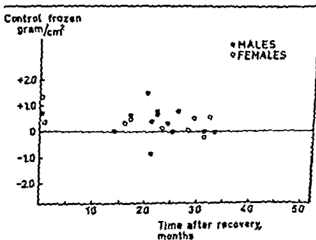


Fig 15
Degree of osteopenia in primary frozen shoulders as a function of time after recovery

In the cases of F S there was a significant decrease of bone mass in the affected side as compared to the unaffected one The average difference amounted to about 50 % of the mineral content of the unaffected side (Fig 12) There was no evidence that the degree of osteopenia associated with F.S was age dependant (Fig 13) nor that it increased with an extended duration of the condition (Fig 14) There was no evidence of restoration of the mineral mass with time (Fig 15)

B TURNOVER OF ^{85}SR[1]

1 Material and Methods

Fifteen cases suffering from unilateral Primary F S 7 men and 8 women, were included in this study Another 6 unilateral but recovered cases 2 men and 4 women were included They had recovered from their F S 9 months to 4 years before the measurement and had regained full range of motion and normal function of their shoulder joints For reference 8 individuals 3 men and 5 women without history or clinical signs of symptoms of shoulder disease or injury were measured Another 6 references 5 men and 1 woman with pain in one shoulder for 3 months or more but without decreased range of motion were measured The age of references and F.S cases was about the same

All the patients were injected intravenously with 50 μCi of $^{85}Sr(NO_3)_2$ Two weeks later the activity was recorded over the shoulder and over the elbow using a lead shielded scintillation detector with a 12° wide angle collimator (diameter of outer aperture 65 mm) The geometry of the detector in relation to the shoulder joint is shown in Figure 16 The uptake in the elbow was measured with the detector in skin contact facing the lateral aspect of the joint

For evaluation of the changes in uptake a ratio was formed between the background corrected count rates obtained from the affected and the unaffected limbs respectively (Fig 17)

2 Results

The uptake in Primary F S was significantly increased when compared to the reference cases In ca es who had restored their range of motion the uptake was significantly decreased as compared to the current cases (Tab

[1] The investig tion was carried out in the Department of Nuclear Medicine, General Hosp tal, Malmo (Head B Nosslin, M D)

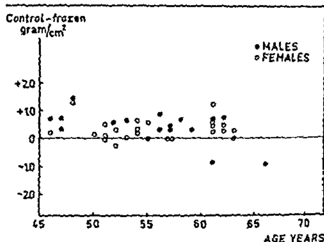


Fig 13
Degree of osteopenia in primary frozen shoulders as a function of age

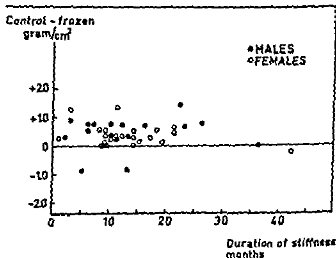


Fig 14
Degree of osteopenia in primary frozen shoulders as a function of the duration of stiffness

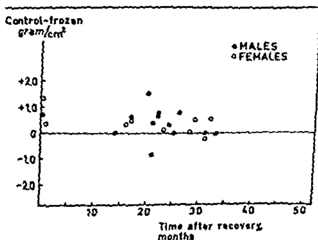


Fig 15
Degree of osteopenia in primary frozen shoulders as a function of time after recovery

APPENDIX

A. REPRODUCTIONS OF RADIOGRAMS AND MICROSCOPY PHOTOGRAPHS

le VII) In painful shoulders without decreased range of motion the up take did not exceed that of the other reference group

There was also some indication of increased uptake in the elbow region of the F S affected limb Again the uptake in the restored cases was significantly less (Table VIII)

There was no difference between men and women in either group

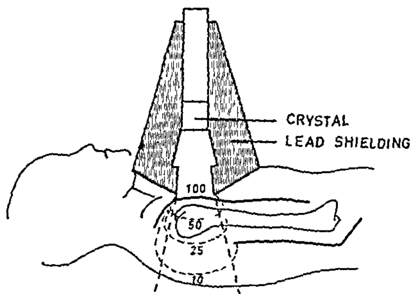


Fig 16
The detector positioned over the shoulder The isoresponse areas shown in relation to the upper end of the humerus

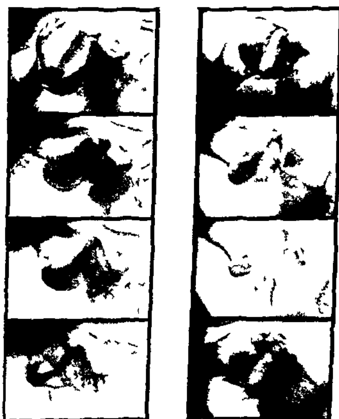
Comment

Within a few months after a tibial shaft fracture a loss of mineral in the knee region of about 25 % has been demonstrated (Nilsson 1966) At the same time the uptake of ^{85}Sr in the same area is usually about quadrupled (Wendeberg 1961) These findings indicate a primary loss of bone due to resorption followed by a response of increased bone formation as evaluated from the ^{85}Sr uptake In the present study the loss of bone exceeds that found in the knee region following fracture and is much greater than could be expected from immobilization so far nobody has been able to demonstrate a convincing local osteopenia in man as a result of immobilization only A joint affection such as a tear of the semilunar cartilage results in a loss of no more than 10 % of the bone mass (Nilsson and Westlin 1968) The loss of bone associated with F S , 50 % is therefore remarkably large

If the continuous loss of bone is taken into account, the initial uptake



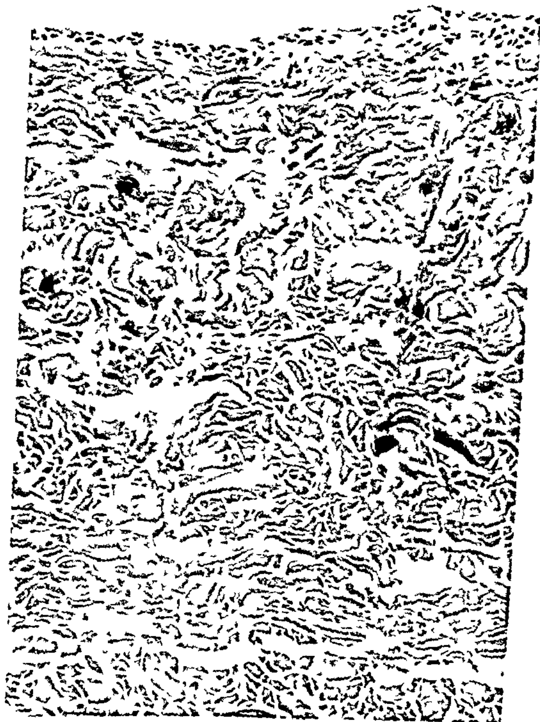
houl l rs as l one second ry to fr cture of the neck of the humerus (right) The varying j nt ol l ter tion. B twe n the second nd the third frames the joint has been released



Appendix X 1
Discontinuous pictures from cinearthrography of one normal (left) three primary frozen quality of the copies is inherent in the method *The first frames of frozen shoulders how* by manipulation and in the last frames extraarticular contrast is more or less visible



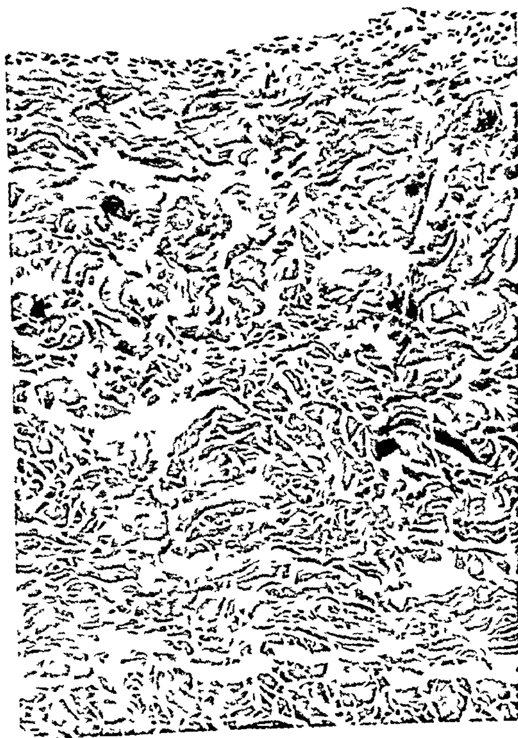
h. uld r and r e secondary to *fracture* of the neck of the humerus (right) The varying j t al.lit ration Between the second and the third frames the joint has been released



Appendix A 2
Histological sections of a normal (left) and a frozen shoulder joint capsule (right). Synovial in the pathological case (Htx eo in 300)



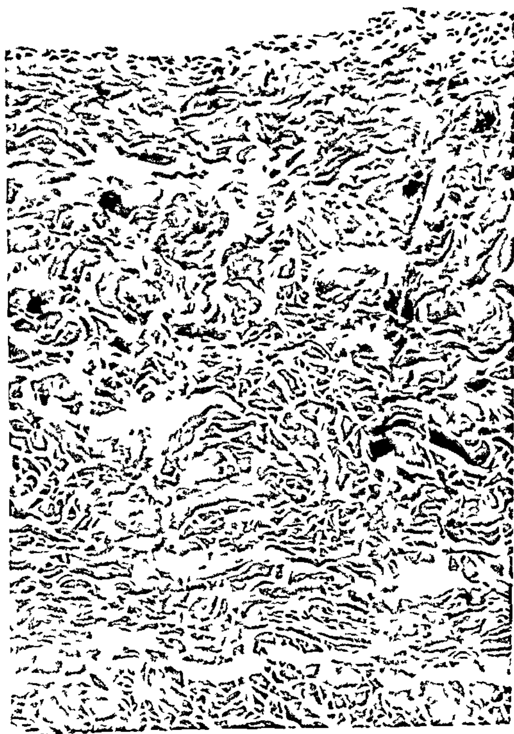
I n ng on t (n the f gures. N te f b op l a d n eness and vascul rity of the fibrous layer



Appendix A 2
Histological ections of a normal (left) and a frozen houlder joint cap ule (right) Synovial in the pathological ca e (Htx eosin × 300)



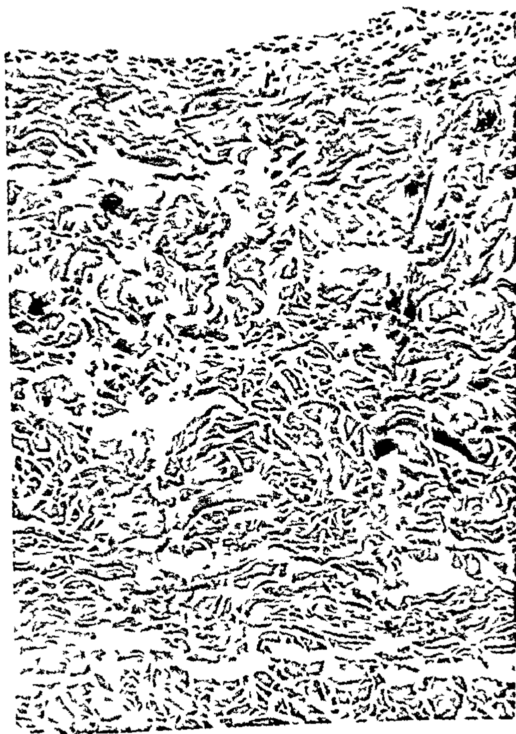
In g nt p in the figure Note fibroblast denseness and vascularity of the fibrous layer



Appendix A 2
Histological sections of a normal (left) and a frozen shoulder joint capsule (right). Synovial in the pathological case (Htx eosin × 300)



l n ng on te] in the f gure Note fibropl ia den eness and va cularity of the fibrous layer



Appendix A 2
Histological sections of a normal (left) and a frozen shoulder joint capsule (right). Synovial in the pathological case. (Htx eosin 300.)



d a f z n houlder j int e j ule (ri ht) Except f r a more compact arrangement of the coll g (16 000)



Apj endix A 3
Electron micro copy in most a pects repre entative of the finding in a normal (left) bundle in the latter pecimen their are no vi ible change in the ultra tructure of the



a id frozen hould e j t t caj ule (ri ht) Except for a more compact arran,ement of the coll gen (16 000)



Appendix A 3

Electron microscopy in most aspects representative of the findings in a normal (left) bundles in the latter specimen their are no visible changes in *the ultrastructure of the*

B STATISTICAL METHODS

For comparison of frequencies the method of Chi square with Yates correction was used

For comparison between sets of numerical data and between paired data the method of t test was used differences in variance in the sets being taken into consideration Skewed distributions were also compared using the geometric means and standard deviations

If interaction from variables other than the tested could be expected, analysis of covariance was used with the interacting variable as the co variant factor even if no significant correlation was found between the two variables

Correlation was calculated as the linear correlation coefficient

Differences and correlations have been referred to as significant when the level of probability was less than 5 %

The central tendency and the scatter of the data were represented as arithmetic Average±Standard Deviation unless otherwise stated.

B STATISTICAL M[illegible]

For comparison of frequencies the [illegible] correction was used.

For comparison between sets of [illegible] the method of t test was used, [illegible] taken into consideration Skewed [illegible] the geometric means and standard [illegible]

If interaction from variables other [illegible] analysis of covariance was used with the [illegible] variant factor even if no significant [illegible] two variables

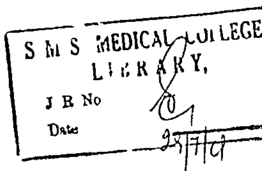
Correlation was calculated as the [illegible]

Differences and correlations have [illegible] the level of probability was less than [illegible]

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The Clinical Appearance of Low Back Disorders in the City of Gothenburg, Sweden

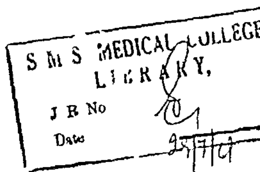
Comparisons of Incapacitated Probands with Matched Controls



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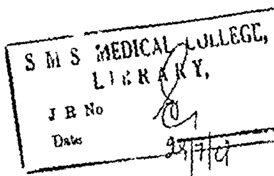
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From the Department of Orthopaedic Surgery University of Gothenburg Sweden
(head. Professor Carl Hirsch)

The Clinical Appearance of Low Back Disorders in the City of Gothenburg, Sweden

Comparisons of Incapacitated Probands with Matched Controls

BY

JIRI HORAL

MUNKSGAARD COPENHAGEN 1969

CONTENTS

A PREFACE

During my training in Bratislava with Professor Cervenansky and in practice as head of the Orthopaedic Department in Liberec, Low Back Pain always was a main interest

Professor Carl Hirsch was at that time by reputation a well known name to me and I was all the happier to be able to work with him when I came to Sweden in 1965 Since then he has been my appreciated chief at the Orthopaedic Department at Sahlgrenska Sjukhuset in Gothenburg From the depth of my heart I thank him for helping me to get started in Sweden and for his encouragement and advice during all phases of this investigation

At the request of Arbetsmarknadens Forsakringsaktiebolag (the Industrial Labour Market Insurance Company) and after consultation with Professors C. Hirsch B Lindegård and H Hyrenius about the necessity of gathering further information about the somatic pattern of disease and the social problems involved in pain of the spine Professor Hirsch requested me to study the somatic problem Doctor Claes Goran Westrin was entrusted with the analysis of the socio-medical problems I am extremely grateful to Professors C. Hirsch B Lindegard and H Hyrenius who have enabled me to fulfil my study and publish the results *I also wish to include Doctor Claes Goran Westrin in these* acknowledgements

I am deeply indebted to Esbjorn Carlstrom Ph D Department of Statistics University of Gothenburg for his invaluable help in planning the statistical analysis My thanks go to Ass Professor Sven Scheller and Doctor Olof Blom for organizing the radiographic examination and interpretation of the radiographs to Miss Ingegerd Jansson (Goteborgs Datacentral for Forskning och Hogre Utbildning) responsible for the data processing work Mrs Inga Lisa Elzer for making the diagrams and Mrs Birgitta Pande for secretarial help

I wish to thank Ass Professor Svante Rolander for all his valuable help in constructive criticism and much appreciated advice

The investigation was made possible by generous grants from Arbetsmarknadens Forsakringsaktiebolag and the Medical Association of Gothenburg

Gothenburg in February 1969

JIRI HORAL

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On the other hand it is known that degeneration of a disc frequently occurs also among subjects who had never experienced low back pain (*Biström* 1954 *Hirsch* 1955) Consequently if lumbar symptoms are caused by changes in a disc the pain mechanism itself remains to be investigated. [2])

There are various types of low back disorders [3])

Even if anatomical pathological and physiological investigations point to the disc being the source of back pain, it is believed that patho-physiological complex combinations are involved (*Barr* 1951 *Hirsch* 1965) [4])

This investigation was begun *in order* to study clinically and roentgenologically two statistically comparable populations They were differentiated at the selection merely by the fact that *one group included those reported sick by a* physician due to low back disorders the other group had not been sick listed. *The purpose of this investigation was mainly to determine the frequency* and the development of different types of low back disorders and to compare the various subjective symptoms with the objective findings

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B INTRODUCTION

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In the 1930 s a compilation of earlier findings could be made on the etiologi of sciatic pain *Mixter et Barr* (1934) contributed by proving that prolapsus of a disc was a common cause of sciatica [2])

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D SURVEY OF LITERATURE

The compiled series of patients with low back disorders revealed the various types of spinal disorders and their medical importance in general as well as socially Comparisons were made between past histories clinical and roentgenological findings Certain anatomical elements of the lumbar spine had been subject to morphological physiological biochemical and biomechanical analyses and assessments Numerous clinical series consist of selected patients who due to spinal disease consulted at orthopaedic clinics (*Hellaeg* 1920 *Jansen* 1926 *Yeoman* 1928 *Stenstrom* 1931 *Friberg* 1939 *Bradford et Spurling* 1939 *Friberg* 1941 *Meyerding* 1941 *Bradford et Spurling* 1947 *Falconer McGeorg et Begg* 1948 *Friberg et Hirsch* (1949) *Soderberg* 1956 *Rettig* 1959 *Sparup* 1960)

Other authors carried out investigations on various groups of the population (*Unander Scharin* 1950 *Hult* 1954 a b *Hult et Forssman* 1957 *Schiotz* 1957 *Kellgren et Laurence* 1958 *Faxen* 1959 *Lundberg* 1959 *Lokander* 1962 *Blomqvist Bergmark et Lindgren* 1964 *Zeiner Henriksen* 1966 *Lindberg Broman Hansson Vilhelmsson* 1966 *Faxen* 1968 *Hirsch Jonsson et Lewin* 1968) Varying selections of patients and controls often prevented comparisons between different series

Unander Scharin (1950) collected data about patients sick listed for lumbar spine disorders at the Stockholm City Central Sick Benefit Society and at the Stockholm Tramway Company Out of the total sick listed during 1948 and belonging to one of the above mentioned groups 4 5 per cent had low back pain or sciatica

Hult (1954 a b) performed an investigation to detect existing cases of spinal disorders of two populations His Munkfors Investigation comprised 100 boys aged 8—11 years 100 apprentices aged 15—20 years 114 woodsmen and 163 industrial workers aged 35—39 years His monography Cervical Dorsal and Lumbar Spinal Syndrome" was based upon 1193 labourers aged between 25—59 years with light and heavy work Wry neck brachialgia and lumbar syndrome were frequently found among the examined subjects Cervicalgia and/or brachialgia had a frequency of 50 6 per cent in subjects with light work and of 51 1 per cent in those with heavy labour Lumbar syndrome occurred in 52 7 per cent among the light workers and among those with heavy labour the figure was 64 4 per cent In the Munkfors-Investigation" low back disturbances amounted to 79 9 per cent while thoracic spine disorders only reached about 5 per cent The author pointed out a correlation between roentgenological findings and cervical and lumbar spine disturbances but no correlation between spinal disorders and various physical build or moderate deformities in the spine or the lower extremities

C INVESTIGATIONAL PROBLEMS

This investigation deals with the following questions

Which are the differences between patients sick listed earlier for low back disorders *(probands)* and previously non sick listed subjects *(controls)* regarding

1 Different types of low back disorders
2 Symptoms of various low back disturbances and their correlation
3 Recurrence
4 Subjective experience of low back disorders
5 Objective findings on examination
6 Presence of cervical — and thoracic spine disorders
7 Roentgenological findings
8 Prognosis of various types of low back disorders

days during this period 15 19 per cent males 9 98 per cent gainfully employed females and 4 35 per cent housewives were subjected to thoracic and lumbar spine disorders

Hirsch Jonsson et Lewin (1968) interviewed 692 females in three of the Gothenburg districts which statistically represented the female population of the country Among those there was lumbar spinal disorders in 49 per cent The development of different types of lumbar spine disorders age at onset and number of recurrences was stated The reliability of the past history was checked at rerewed in erviews

Many of the cl nical studies also include radiographic changes found in the series to be inves gated The authors were mainly interested in existing degeneration of the disc deforming spondylosis and congenital spinal changes

Badgley (1937) found that a reduction of the lower lumbar intervertebral spaces occurred more often in patients with sciatica than with lumbago

Hodges et Peck (1937) who compared Badgley s cases with a larger number of controls found sig ificantly more often a reduced intervertebral space in patients with lumbago and sciatica than in the controls (4 5 1) the same phenomenon applied to congenital anomalies (2 1) Contrary to this spondylarthritis was found rather often in the controls as compared to the patients The importance of the investigation becomes reduced however as the controls were not statistically matched with the patients suffering from lumbago and sciatica Their mean age was slightly lower and they had come to the clinic because of spinal disorders but of a different type to lumbago and sciatica

Severin (1943) examined 210 patients with degeneration of the lumbar discs which had been verified roentgenologically No other changes were observed on the radiographs The greatest frequency of degeneration of the disc was found by the author to occur between 31 and 55 years The severity of the disc degeneration in his material did not show any parallelism with age *Bistrom* (1954) examined 151 individuals with a healthy spine and found that spondylosis clearly depended on the age and occurred earlier in males than in females Spondylolisthesis and spondylolysis were found in 14 3 per cent, transitional vertebrae in 20 per cent asymmetrical transitional vertebrae in 6 6 per cent.

Hult (1954 a b) stated that degeneration of a disc depends on the age and can be regarded as a physiologic process

Much attention was given roentgenologically verified and clinically important congenital changes of the spine *Hibbs et Swift* (1929) stated that congenital changes cause instability which result in spinal disorders *Willis* (1932) wrote that congenital changes and asymmetrical sacralization and lumbarization are of clinical interest due to reduced resistance in damage or disease Later (1941) he found a greater inciden e of anomalies in cases with aching lumbar spine than in those without symptoms *Ingelrigtsen* (1937) believed that asymmetrical sacralization is of great pathogenetic importance in spinal disorders In his series of patients

Low back pain was more often found in manual workers but the author mentions that the work in itself cannot be the cause of the spinal disease

Schiotz (1957) found in the Oslo Trygdvekasse that of the total number of sick days, low back pain and sciatica amounted to 7 3 per cent

Kellgren et Laurence (1958) clinically and radiographically, examined a series selected at random in a British town (Leigh), 170 males and 145 females aged between 55—64 years In males of this comparatively high age there were cervical and lumbar degeneration of the discs in 69—83 per cent and the females revealed a percentage of between 52—72 per cent

Faxen (1959) in checking the local branch of the National Health Insurance Service in suburban areas of Gothenburg during 1955—1957 found that spinal disease in males amounted to 11 74 per cent of all the sick cases and 15 per cent of all days lost through illness, and was merely surpassed by upper respiratory infections In females the corresponding figures were 5 53 per cent of all sick cases and 8 36 per cent of all days lost through illness, and thus held the third place after psychic insufficiency and upper respiratory infections

Lindberg (1959) stated that 9 per cent of all the days lost through sickness depended on spinal disorders The author calculated on the compensation merely for spinal disorders to the population of Gothenburg (397 205 subjects) amounting to more than 4 mill Sw Kr in 1958

Lokander (1962) stated that at ASEA in Vasteras the spinal disorders amounted to 20 per cent of the total number of days lost through sickness

Zeiner Henriksen (1966) studied the rate of sick listed members and the morbidity among male patients with sciatica belonging to the Oslo Health Insurance He excluded those who were hospitalized on the diagnosis sciatica For comparison a control group was used which however was not matched with the patients He proved that patients with sciatica more often had nervous or psychic disturbances and alcohol problems than their control group Furthermore patients subjected to surgery had a less number of morbid conditions than those conservatively treated *Lindberg Broman Hansson Vilhelmsson* (1964) found that the city of Gothenburg with a population of 418 600 had 17 000 persons aged between 16—64 years who suffered from spinal disease This figure exceeds the number of patients with heart insufficiency by four and is twice the number of other diseases in the extremities as known to the National Health Insurance Office By including other localization of spinal disease the figure increases to 22 000 patients who were aged between 16 and 24 years during 1964 in Gothenburg the females constituting 50 8 per cent Only 13 6 per cent of these patients were capable of work despite continued symptoms 36 8 per cent were sick listed for more than 90 days The authors maintained that 50 per cent of the patients with spinal disease ought to have medical attendance

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ERRATA

Page 18	Age groups 20–29 10 9 read 10 8 Age groups 60–69 18 4 read 18 0
Page 19	Table 1 On Examination 1962 read 1967
Page 43	Line No 15 Read Incidence of thoracic spine syndromes with/without radiating pain.

with lumbar spine disorders *Brofeldt* (1937) reported a high frequency of asymmetrical sacralization with scoliosis (18 1 %) and spondylolisthesis and spondylolysis (21 5 %) *Friberg* (1939) found sacralization in 5 3 per cent hemivertebra in 1 6 per cent, spondylolisthesis and spondylolysis in 6 3 per cent and other congenital changes in 2 4 per cent *Muralt* (1949) in his series of 124 patients who were operated for prolapsus of a disc reported sacralization in 15 3 per cent *Rettig* (1959) believed that slight disturbance in the development of the lumbar and sacral spine rarely causes inconvenience, but that by no means must it be disregarded due to reduced resistance and a predisposition for spinal disorders as a result *Makovicky* (1963) found congenital changes of the vertebrae in 45 per cent of the examined subjects selected at random

There are great variations in the literature as regards the etiology The various principles of selection when collecting clinical data are also responsible for the calculation of spinal symptoms

E METHODS

1 Selection of Series and Statistical Analysis

This investigation deals with a series which was selected with the intention of elucidating it from both the socio-medical and orthopaedic points of view. Consequently, a group selected at random and sick listed due to low back disorders — *probands* — was compared with a matched group of individuals — *controls* — who had not been sick listed during the period from 1st January 1955 until 1st January 1967. The investigation began in 1966. The probands were selected among those who had been sick listed for low back disorders during 1964.

In reviewing the records of the National Health Insurance Service at Gothenburg, which in 1964 totalled 450 000 inhabitants, it was found that approximately 17 000 persons had been incapable of work for long or short periods due to spinal disorders. The number of patients reported sick by their physicians was considerably less, however, and amounted to about 9 000 persons. From the latter group random selections were made of those born on the first day of each month.

Notice: In Sweden each member of the National Health Insurance can report his or her illness over the telephone without having to produce a doctor's certificate. This type of "self-sick listing" is valid no longer than one week. Starting from January 1st 1967 compensation is paid as from the first day of sick listing. Previously a waiting period of three days elapsed and from the fourth day compensation was paid out. Should the patient consider it necessary for him to extend his period of sick listing, a doctor's certificate must be produced at the end of the first week.

The group of probands consists of patients sick listed by physicians in 1964 for lumbar spine disorders during at least one week. Only those with a diagnosis of primary spinal disorders were regarded as probands, while those with any other disease were excluded, even if lumbar spine disorders were present as a second diagnosis. For practical and statistical reasons it was decided that only Swedish born members would be included. The number of primary selected probands was 277. Five of the probands died after 1964 and three moved elsewhere. Some refused to partake in the examination and thus the proband series comprised 243 individuals, which was 87.7 per cent of the original number and 90.3 per cent of those summoned. Each selected proband was "matched" with a *control* who corresponded with regard to sex, age and sickness benefit *category* (— income). The controls had not been reported sick by a doctor for lumbar spine disorders from 1955, at which time the National Health Service began, until 1st January 1967 when the actual investigation was commenced.

1 Selection of Series and Statistical Analysis

This investigation deals with a series which was selected with the intention of elucidating it from both the socio-medical and orthopaedic points of view Consequently, a group elected at random and sick listed due to low back disorders — *probands* — was compared with a matched group of individuals — *controls* — who had not been sick listed during the period from 1st January 1955 until 1st January 1967 The investigation began in 1966 The probands were selected among those who had been sick listed for low back disorders during 1964

In reviewing the records of the National Health Insurance Service at Gothenburg which in 1964 totalled 450 000 inhabitants it was found that approximately 17 000 persons had been incapable of work for long or short periods due to spinal disorders The number of patients reported sick by their physicians was considerably less however and amounted to about 9 000 persons From the latter group random selections were made of those born on the first day of each month

Notice In Sweden each member of the National Health Insurance can report his or her illness over the telephone without having to produce a doctor's certificate This type of self sick listing is valid no longer than one week. Starting from January 1st 1967 compensation is paid as from the first day of sick listing Previously a waiting period of three days elapsed and from the fourth day compensation was paid out. Should the patient consider it necessary for him to extend his period of sick listing a doctor's certificate must be produced at the end of the first week

The group of probands consists of patients sick listed by physicians in 1964 for lumbar spine disorders during at least one week Only those with a diagnosis of primary spinal disorders were regarded as proband while those with any other disease were excluded even if lumbar spine disorders were present as a second diagnosis For practical and statistical reasons it was decided that only Swedish born members would be included The number of primary selected probands was 277 Five of the probands died after 1964 and three moved elsewhere Some refused to partake in the examination and thus the proband series comprised 243 individuals which was 87.7 per cent of the original number and 90 3 per cent of those summoned Each selected proband was matched with a control who corresponded with regard to sex age and sickness benefit category (= income) The controls had not been reported sick by a doctor for lumbar spine disorders from 1955 at which time the National Health Service began until 1st January 1967 when the actual investigation was commenced

Out of 269 controls 235 were willing to partake in this investigation (87 4 %) Due to non response in both groups, 424 individuals were available, viz 212 matched pairs for comparison which constituted 76 6 per cent of all the primarily selected probands and 78 8 per cent of all the primarily selected controls The others were excluded from the investigation Each group of probands and controls included 125 males (59 %) and 87 females (41 %)

The series classified in groups of probands and controls gave a selection which permitted statistical analyses and comparisons, and enabled the problems of this investigation to be dealt with Controls with previous lumbar spine disorders and those without previous symptoms could be compared with each other and with the probands with which they were matched

After the author personally had examined each of the 424 subjects, all the results were transferred to a code system and then to a punch card (272 columns for each subject) for data processing The data obtained were tabulated and various groups and classifications were statistically analysed, where the probabilities were expressed in chi square (X^2) or the t test together with Degree of Freedom (d f) Only significant X — or t test values were included When calculating the mean values and the mean ages, the Standard Error (SE) was given In most of the tables both absolute figures and percentage are indicated

2 Clinical Examination

In order to avoid subjective bias the author at the time of examination in 1967 was unaware of the fact whether the subject was a control or a proband When the entire series had been examined this piece of information was added to the code system For the same reason the examination was first made without previous knowledge of the past history Afterwards the past history was enquired into and included in the code system together with the findings At the examination several techniques were used as described by the American Academy of Orthopedic Surgery (1965) *Simmons* (1966) and by *Hirsch* and *Hult* in Chapters 15 and 16 respectively of Nordisk Larobok i Ortopedi (Scandinavian Textbook of Orthopaedic Surgery 1959)

The examination began with inspection of the general condition body structure gait obvious deformities and detailed examination of extremities and spine followed by palpation of the latter parts Special attention was paid to tenderness in spinal processes and to the paravertebral musculature both in standing and reclining positions Any deviation of the pelvis was measured The function of the extremities and the spine was examined differences in symmetry measured and distance between finger tips and floor at maximal flexion of back and hip joints was noted Conclusively the upper and lower extremities were subjected to neurological examination Merely results of statistical value or of some clinical importance were included

3 Case History

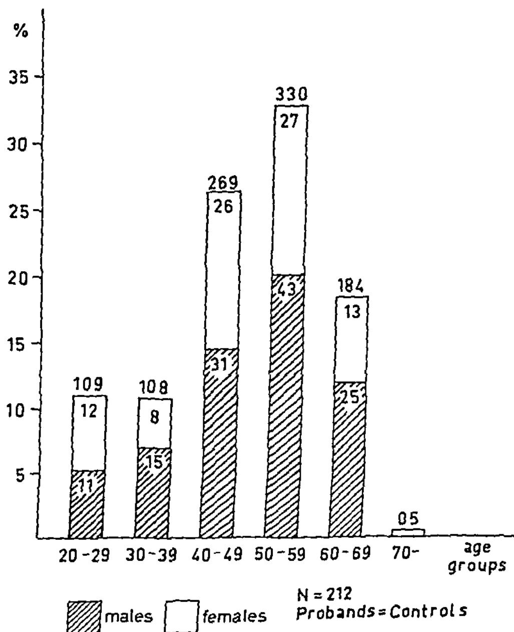
Previously arranged questions were asked by the author and noted The subjects were first asked about existing low back pain As *Howorth* (1962) mentions by beginning with questions which are of interest to the patients it will be easier to bring out a more reliable past history When the subject admitted to symptoms they were asked about their opinion of the cause character localization, intensity and whether they experienced restriction of movement in connection with low back pain Enquiries were then made about details as to the onset, number of recurrences and possible symptoms in 1964 At the examination a question was asked whether or not the subject had had any lumbar spine disorder during the past three or four years Questions regarding the precise time of illness could cause a lapse of memory by the subject and were consequently not predominant. Both probands and controls were questioned as to previous symptoms from the cervical and thoracic spine When the examination was completed a diagnostic summary was made both retrospectively and on the basis of the past history only and clinically on the basis of the objective findings and symptoms on examination in 1967

4 Reliability of Past History and Sources of Error

The past history is based upon the subjects own history which should be taken cum grano salis *(Magnusson* 1968) Lapse of memory and imaginary symptoms can never be quite excluded *Blomqvist Bergmark et Lindgren* (1962) showed on examination of patients sick listed during at least 90 days in Stockholm Gothenburg Malmo and Norrkoping that the diagnosis in the doctor s report to the National Health Service, as a rule always can be accepted

In a later investigation of joint subjects *Westrin* (to be published) will analyse the reliability of past histories as stated to the author and himself on different occasions and the sources of error Thus he will prove that the past history in some cases is reliable in others it deviates

Fig 1 Number and Percentage of Subjects in the Various Age Groups



1 Age Distribution

The series included 424 examined subjects There were 125 males and 87 females together 212 probands and an equal number of matched controls The mean age of both probands and controls at the time of examination in 1967 was for males 49 48 ± 1 07 years and for females 47 71 ± 1 34 years *There was no significant statistical deviation*

In this series the morbidity of males and females increases up to the age of between 50 and 59 years even if the increase in morbidity of females as compared *to the age group* 40—49 years only was 6 1 per cent (1 individual) Then the mor bidity rapidly declines There was a slight decrease in the number of females in the ages between 30 and 39 years of age probably due to the small number of examined subjects in this age group One female proband and one female control had reached the age of 71 years at the time of examination The proband, however was sick listed in 1964 because of low back pain.

2 Definition of Slight and Intense Pain/Ache

It is impossible to determine the degree of ache without prejudice, as it is a subjective sensation The subjects were asked to give as detailed a definition as possible about their sensation of pain The more or less synonymous expressions which were used are

TABLE 1 Subjective Sensation of Pain on Various Occasions

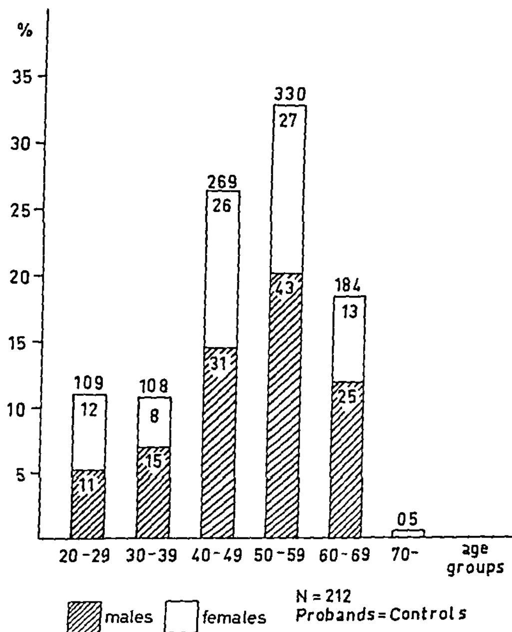
	Onset				*Majority of Recurrences*			
	P		C		P		C	%
Intense p in	156	73 9	79	56 0	79	41 6	25	26 6
No intense p in	55	26 1	62	44 0	111	58 4	69	73 4
Total	211	100 0	141	100 0	190	100 0	94	100 0

$(X^2 = 12\ 21^{***}\ d\ f = 1)$ $(X^2 = 6\ 00^{*}\ d\ f = 1)$

	1964 (1963—1966)				On Examination 1962			
	P		C		P		C	%
Intense pain	147	69 7	30	33 0	13	12.0	1	1 8
No intense pain	64	30.3	61	67 0	95	88 0	55	98 2
Total	211	100 0	91	100 0	108	100 0	56	100 0

$(X^2 = 35\ 30^{***}\ d\ f = 1)$ $(X^2 = 4\ 96^{*}\ d\ f = 1)$

Fig 1 Number and Percentage of Subjects in the Various Age Groups



On some occasion intense pain/ache in the lumbar spine had been experienced by 177 probands (83 9 %) and 90 controls (63 8 %) 156 probands (73 9 % of the entire series) and 79 controls (56 % of all subjects with previous spinal disorders) had experienced intense pain at the onset However only 37 4 per cent of the probands and 12 7 per cent of the controls with lumbar spine disorders had had the same sensation at most of the recurrences

The results show that 50 6 pe ent of the probands who claimed intense pain at the onset had the same sensation also at most of the recurrences On the other hand only 22.8 per cent of the controls had the same sensation at onset and recurrence. The difference is statistically significant ($X^2=7$ 23** d f =1)

If the above results are compared with Table 1 it is found that all the *probands who had intense pain at mo t of the recurrences* also experienced this at the onset of low back disorders Out of 25 controls with intense pain at most of the recurrences 72 per cent mentioned that they had intense pain at the time of onset

Correlation between intensity of pain and consultation with physician

All the probands consulted a physician due to low back pain, but only 72 (51 1 %) of the controls The difference is statistically significant ($X^2=125$ 11*** d f =1) Out of the 90 controls who at some time had experienced intense pain/ache in the lumbar spine 69 consulted a physician Out of 51 who only had slight pain/ache in the lumbar spine three consulted a physician ($X^2=44$ 83*** d f = 1 $X^2=73$ 51*** d.f =1) applies to both cases and to the probands and the ontrols respectively and is statistically highly significant.

The controls who had experienced intense pain in the lumbar spine were asked why they had not consulted a physician Most of them answered that they had not considered their illness as serious and were very busy with their work or that they had tried pain relieving pills rest and possibly a few days of sick leave The same answer was given by a female control who had objective signs of sciatica at the time of examination in 1967

Consulted physician according to distribution of lumbar spine diagnoses at the exam nation 1967 — see separate Table 2

Summary In studying the development and duration of pain the probands as compared to the controls have a tatistically significant higher frequency of low back pain which they experienced as intense both at the time of onset and at the recurrences The controls even *in connection* with intense pain often had not consulted a physician and almost never when the pain was slight.

Sensation of low back pain

The development and duration of low back pain at the onset in 1964 and at the time of investigation in 1967 was studied in detail

1 Solid pain 2 Intense pain 3 Flashing pain 4 Sharp pain 5 Spasmodic pain 6 Terrific pain 7 Feels like a boil 8 Intense dull pain 9 Feeling of discomfort 10 Feeling of exhaustion 11 Feeling of stiffness 12 Slight pressing pain 13 Mild dull pain 14 Insignificant pain Using a somewhat arbitrary estimation, Nos 1—8 were included into one group under the designation intense pain/ache and the remaining were called slight pain/ache

A statistically significant larger group of probands as compared to the controls claimed intense pain/ache at each examination The significance of low back pain was greatest in 1964, and lowest at the examination

The probands and controls who at the onset of low back pain claimed intense and slight pain/ache respectively were compared with respect to their age

TABLE 2 Degree of Pain at First Onset

	Intense pain/ache at first onset				Slight pain/ache at first onset			
	P	%	C		P	%	C	%
0–19	20	12 8	6	7 6	9	16 4	4	6 5
20–29	34	21 2	28	35 4	10	18 0	19	30 7
30–39	42	26 9	23	29 1	14	25 6	18	29 0
40–49	35	23 1	13	16 5	15	27 3	11	17 7
50–59	20	12 8	8	10 1	7	12 7	7	11 3
60–69	5	3 2	1	1 3	–		3	4 8
70–	–		–		–		–	
Total	156	100 0	79	100 0	55	100 0	62	100 0

Mean age ± SE
P = 35 51 ± 1 15 years
C = 33 61 ± 1 38

Mean age ± SE
P = 34 36 ± 1 92 years
C = 35 81 ± 1 99

There were no significant differences in the mean age and the age distribution in comparison with the probands and the controls Similar results were found also in the age distribution of those who claimed intense and slight pain/ache respectively in connection with most of the recurrences and around 1964

A statistically significant higher frequency of intense pain sensation in subjects earlier sick listed for low back pain justified an investigation The aim was to find out the prognostic value of pain sensation and also to determine whether the subject in connection with recurrences experienced pain of the same intensity

Most of the cases of sciatica (45 %) were found among the probands in 1964 The greatest number of controls with sciatica (21 9 %) occurred at the time of onset In both groups the lowest frequency of sciatica diagnosed at the time of examination in 1967 was 22 2 per cent among the probands and 10 7 per cent among the controls

Sciatica occurred in a statistically significant higher degree among the probands sick listed in 1964 than among the controls who were not sick listed ($X^2 = 17.3^{***}$ d f = 1) The X^2 test of the recurrences is not statistically significant.

Summary Low back pain and sciatica was found in probands and controls on different occasions Even if the memory had slipped some of the subjects the collected data seem to be logical however The greatest number of cases of sciatica was found in the probands in 1964 i e the time at which all were sick listed The controls experienced the most intense pain at the onset of the disease mostly before 1955 when their illnesses were not yet recorded at the National Health Service When discussing the development and duration of pain it was pointed out that most of the probands and the controls had experienced the onset of low back disorders as the most severe attack A combined sensation of intense pain and radiating pain/ache, therefore is not surprising

3 Definition of Various Low Back Disorders (Low Back Insufficiency, Lumbago, Sciatica)

Based upon the past history and on the first symptoms the subjects were classified in four groups previously healthy low back insufficiency lumbago and sciatica

The variations in the disease during numerous recurrences were followed up from the onset and in 1964 at which time the probands were sick listed up to the first six months of 1967 when the examination took place

Low back insufficiency included sensation of tiredness weakness stiffness and dull pain in the back The signs may vary in intensity and duration and may be connected with any stress to which the spine is subjected

Lumbago is characterized by an acute localized pain or ache which appears at the onset in the lumbar spine with restricted movement as a result

Sciatica can be recognized by radiating pain/ache of a radicular kind in the legs The intensity of the pain varies and other symptoms such as a feeling of weakness of the legs paraesthesia and a sensation of numbness o cur All the groups were classified in so-called "consistency cases and "variations" As consistency cases" were regarded subjects who from the time of onset until the time of examination only had one and the same type of low back disorder In cases where the pattern varied e g from sciatica to lumbar spine insufficiency or from lumbago to sciatica the term "variations of sciatica with lumbar spine insufficiency and variation of lumbago with sciatica was employed

TABLE 3 Sensation of Low Back Pain

	Low Back Pain at Onset		Around 1964		On Examination in 1967	
	P	C	P	C	P	C
Pain day and night	115	48	100	15	13	1
Only with movement	61	53	67	32	18	9
Only with strain	22	29	28	32	42	23
Other reasons	13	11	16	12	35	23
Total	211	141	211	91	108	56

A statistically significant higher number of probands than controls stated that they had pain day and night at the time of onset and even during the sick listing period in 1964 ($X^2=15\,9^{**}$ d f =3) at the time of onset and ($X^2=33\,7^{***}$ d f =3) during 1964

About half of all the probands mentioned that the pain carried on day and night on both occasions Corresponding data, given by the controls were at the time of onset 34 per cent and 16 5 per cent in 1964

About 40 per cent of both probands and controls at the time of examination experienced pain only in connection with strain, 18 5 per cent of the probands and 26 8 per cent of the controls had pain when standing or sitting for a long time

For further details of the above mentioned chapter and for comparison between subjects with intense — slight pain/ache respectively see separate Table 3

Summary A statistically significant higher frequency of probands as compared to the controls had continuous low back pain both at the time of onset and around 1964 Low back pain in connection with certain movements or strain occurred more often among the controls than the probands

Localization of pain

The past history revealed how often the symptoms were localized only to the lumbar spine and how often sciatica occurred Only characteristic radicular radiating pain was accepted as sciatica

TABLE 4 Localization of Pain

	Onset				Around 1964				On Examinat in 1967			
	P	%	C	%	P	%	C	%	P	%	C	%
Lumbar Sacral Spine	150	71 6	109	78 1	116	55 0	73	80 2	84	77 8	50	89 3
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Based upon the past history and on the first symptoms the subjects were classified in four groups: previously healthy, low back insufficiency, lumbago, and sciatica.

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Total	211	100 0	141	100 0	211	100 0	91	100 0	108	100 0	56	100 0

According to their own statements only 8 probands and none of the controls were incapacitated for work due to low back disorders at the time of examination. A statistically significant greater frequency of probands with previous low back pain and further at the examination in 1967 was noted as compared to the controls. In the control group 66.5 per cent (66.7 % females and 66.4 % males) complained of previous low back pain and 33.5 per cent (33.3 % females and 33.6 % males) had never had any symptoms or signs. Out of the 71 subjects who had never had any low back disorders 40.8 per cent were females and 59.2 per cent males. The distribution of sex in this group was almost identical with those who had low back disorders. The distribution of age in those who had never had symptoms did not differ either when compared with the other subjects. The greatest number of previously symptom free males were aged between 50 and 59 years and the females were between 40 and 49 years of age.

The mean age in males was 48.81 ± 7.14 years and in females 47.24 ± 7.59 years. There is no difference in the figures as compared with those of low back pain symptoms.

TABLE 6. Distribution of Age in Controls According to Past History

Age	Low Back Pain Symptoms		No Symptoms	
	Males	Females	Males	Females
20—29	4	7	7	5
30—39	9	6	6	2
40—49	26	19	5	7
50—59	31	15	12	12
60—69	13	11	12	2
70—	0	0	0	1
Total	83	58	42	29

Of the subjects who had never earlier had low back pain 31 had experienced disorders in the cervical and thoracic spine. The mean age of the remaining 40 controls who had been symptom free in the entire spine was 47.62 ± 7.23 years and included the oldest control, i.e. there was no difference in comparison with other groups. For further details of the above mentioned chapter see separate Table 4.

Summary. The incidence of low back disorders in the present control series is high and includes 66.5 per cent of the controls. This selection is not characteristic of an epidemiological picture of the population, the reason being that the examination was based upon a principle of selection where all cases of lumbar spine disorders which may exist were not included. No difference in sex

When the author guided by the case history of the probands and the controls in different groups of lumbar spine syndrome, attempted to use the terms "lumbago chronicum" and "lumbar spine insufficiency" it was found that lumbago chronicum and spinal insufficiency only in extreme cases could be clearly differentiated In most cases it was very difficult to distinguish between the two groups due to a great overlap when obtaining the symptoms Therefore, the author has included lumbago chronicum in his classification "lumbar spine insufficiency"

"Coaching ache is due to fatigue of the musculature owing to unusual labour When localized in the lumbar spine it has not been regarded as a spinal disease

4 Incidence of Low Back Disorders in Probands and Controls

Back disorders is a general term including all kinds of pain and discomfort in the spine

TABLE 5 Existing Low Back Pain Based Upon Interviews in 1967

	P	%	C	%	
Low Back Pain prior to examination in 1967	211	99 5	141	66 5	(X^2=81 98*** d f =1)
No Low Back Pain prior to examination in 1967	1	0 5	71	33 5	
Total	212	100 0	212	100 0	
Subjects with symptoms also on examin in 1967	108	51 2	56	39 7	(X^2=4 47* d f =1)
Subjects with previous symptoms but without symptoms on examin in 1967	103	48 8	85	60 3	
Total	211	100 0	141	100 0	

211 probands and 141 controls had low back pain prior to but not at the actual examination in 1967 One proband also at the second interview did not admit to spinal disorders no doubt depending on lapse of memory Of those with previous disorders, 51 2 per cent of the probands and 39 7 per cent of the controls had low back pain at the examination in 1967

of the controls There was no statistically significant difference when comparing the subjects who had symptoms The distribution of sex revealed a small significant difference ($X^2=4\ 35^*$ d f =1) between female and male controls

Distribution of age

Th differences in distribution of age between probands and controls in low back disorders are given in Table 7

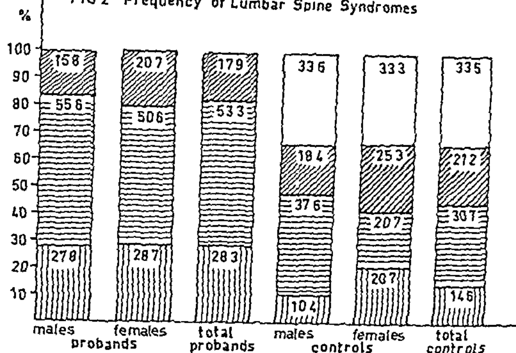
TABLE 7 *Age Dependence of Low Back Disorders*

		20–29	30–39	40–49	50–59	60–71	20–71
Insufficiency	P	9 24 2	4 10 5	8 21 0	10 26 3	7 18.0	38 100 0
	C	5 11 1	9 20 0	16 35.6	7 15 6	8 17 7	45 100 0
Lumbago	P	11 9 7	11 9 7	30 26 5	39 25 7	22 28 4	113 100 0
	C	4 6 2	6 9 2	17 26.2	30 46 1	8 12.3	65 100 0
Sciatica	P	3 5 0	8 13.3	18 30 0	21 35 0	10 16 7	60 100 0
	C	2 6 5	0 –	12 39 0	9 29 0	8 25 5	31 100 0

Low back insufficiency was found to have a high frequency already among the young probands and remained stable after the age of 29 years with the exception of a slight increase in females ranging from 50 to 59 years In the control subjects the increase continued up to the age group of 40—49 years after which it rapidly declined

The frequency of lumbago is comparatively low in the ages from 20—29 years with only 9 7 per cent of probands and 6 2 per cent of controls who had symptoms There was no increase in the probands belonging to the next decade and only a slight increase in the controls The highest frequency of lumbago was found in the probands ranging from 40—49 years and 50—59 years in the controls (26 5 per cent and 46 1 per cent, respectively) After the age of 60 years the probands maintained the same figures but the controls revealed a decrease of only 12 3 per cent.

In the ages 20—29 years only 5 per cent of the probands and 6 5 per cent of the controls with symptoms, had had sciatica The curve then increased for



(cf Table 1 Appendix)

distribution was noted Only 18 8 per cent of the controls stated that they had always been free of symptoms also in other parts of the spine

Among the probands there was one who in his spontaneous past history omitted to mention previous symptoms of low back disorders Out of the controls 42 males and 29 females had not had previous *symptoms In the control group* the mean age in both males and females wa 47 90 + 2 30 years

Lumbar spine insufficiency occurred in 17 9 per cent of the probands and in 21 2 per cent of the controls A statistically significant greater frequency of controls had lumbar spine disorders as compared with the probands (X^2=9 07** d f = 1)

Lumbago was found in 53 3 per cent of the probands and in 30 7 per cent of the controls A comparison of the subjects who merely had symptoms did not reveal any statistically significant differences In lumbago there was a decided statistically significant surplus of males as compared with *female controls* (X = 16 94*** d f = 1)

Sciatica occurred in 28 3 per cent of the probands and in 14 6 per cent

of the controls There was no statistically significant difference when comparing the subjects who had symptoms The distribution of sex revealed a small significant difference ($X^2 = 4\ 35^*$ d.f = 1) between female and male controls

Distribution of age

The differences in distribution of age between probands and controls in low back disorders are given in Table 7

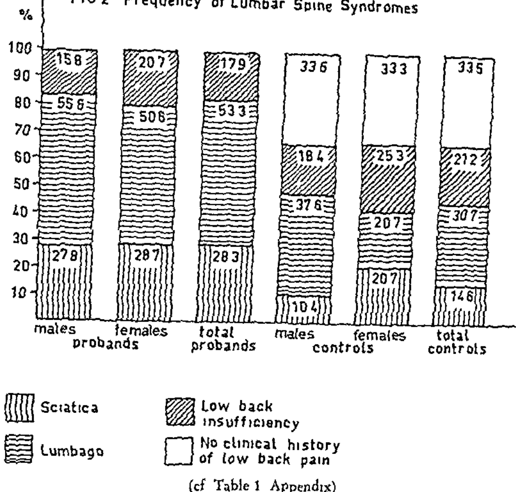
TABLE 7 Age Dependence of Low Back Disorders

		20–29		30–39		40–49		50–59		60–71		20–71	
Insufficiency	P	9	24.2	4	10 5	8	21 0	10	26.3	7	18 0	38	100 0
	C	5	11 1	9	20 0	16	35 6	7	15 6	8	17 7	45	100 0
Lumbago	P	11	9 7	11	9 7	30	26 5	39	25 7	22	[illegible]8 4	113	100 0
	C	4	6 2	6	9.2	17	26.2	30	46 1	8	12.3	65	100 0
Sciatica	P	3	5 0	8	13.3	18	30 0	21	35 0	10	16 7	60	100 0
	C	2	6 5	0	–	12	39 0	9	29 0	8	25 5	31	100 0

Low back insufficiency was found to have a high frequency already among the young probands and remained stable after the age of 29 years with the exception of a slight increase in females ranging from 50 to 59 years In the control subjects the increase continued up to the age group of 40—49 years, after which it rapidly declined

The frequency of lumbago is comparatively low in the ages from 20—29 years with only 9 7 per cent of probands and 6 2 per cent of controls who had symptoms There was no increase in the probands belonging to the next decade and only a slight increase in the controls The highest frequency of lumbago was found in the probands ranging from 40—49 years and 50—59 years in the controls (26 5 per cent and 46 1 per cent respectively) After the age of 60 years the probands maintained the same figures but the controls revealed a decrease of only 12 3 per cent.

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distribution was noted Only 18 8 per cent of the controls stated that they had always been free of symptoms also in other parts of the spine

Among the probands there was one who in his spontaneous past history omitted to mention previous symptoms of low back disorders Out of the controls 42 males and 29 females had not had previous symptoms In the control group the mean age in both males and females was 47 90 ± 2 30 years

Lumbar spine insufficiency occurred in 17 9 per cent of the probands and in 21 2 per cent of the controls A statistically significant greater frequency of controls had lumbar spine disorders as compared with the probands ($\chi^2 = 9\ 07^{**}$ d f = 1)

Lumbago was found in 53 3 per cent of the probands and in 30 7 per cent of the controls A comparison of the subjects who merely had symptoms did not reveal any statistically significant differences In lumbago there was a decided statistically significant surplus of males as compared with female controls ($X^2 = 16\ 94^{***}$ d f = 1)

Sciatica occurred in 28 3 per cent of the probands and in 14 6 per cent

of the controls There was no statistically significant difference when comparing the subjects who had symptoms The distribution of sex revealed a small significant difference ($\chi^2 = 4\ 35^*$ d.f $= 1$) between female and male controls

Distribution of age

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TABLE 7 Age Dependence of Low Back Disorders

		20–29		30–39		40–49		50–59		60–71		20–71	
Ins fficiency	P	9	24 2	4	10 5	8	21 0	10	26 3	7	18 0	38	100 0
	C	5	11 1	9	20 0	16	35 6	7	15 6	8	17 7	45	100 0
Lumbago	P	11	9 7	11	9 7	30	26 5	39	25 7	22	28 4	113	100 0
	C	4	6.2	6	9.2	17	26.2	30	46 1	8	12.3	65	100 0
Sciatica	P	3	5 0	8	13 3	18	30 0	21	35 0	10	16 7	60	100 0
	C	2	6 5	0	–	12	39 0	9	29 0	8	25 5	31	100 0

Low back insufficiency was found to have a high frequency already among the young probands and remained stable after the age of 29 years with the exception of a slight increase in females ranging from 50 to 59 years In the control subjects the increase continued up to the age group of 40—49 years, after which it rapidly declined

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In the ages 20—29 years, only 5 per cent of the probands and 6.5 per cent of the controls with symptoms, had had sciatica. The curve then increased for

the probands in the ages between 50—59 years and for the controls aged 40—49 years Then a marked decrease was found in both groups

Hirsch Jonsson et Lewin (1968) noted the same phenomenae in their female subjects Due to various selections the series cannot be compared in detail with those of the author

TABLE 8 *Frequency of Low Back Disorders within the Different Age Groups*

		20—29		30—39		40—49		50—59		60—71	
Insufficiency	P %	9	39 2	4	17 4	8	14 3	10	28 6	7	18 0
	C %	5	45 4	9	60 0	16	35 5	7	15 2	8	32 2
Lumbago	P %	11	47 8	11	47 8	30	53 6	39	41 4	22	56 4
	C %	4	36 4	6	40 0	17	37 8	30	65 2	8	33 9
Sciatica	P %	3	13 0	8	34 8	18	32 1	21	30 0	10	25 6
	C %	2	18 2	0	—	12	26 7	9	19 6	8	33 9
Total	P %	23	100 0	23	100 0	56	100 0	70	100 0	39	100 0
	C %	11	100 0	15	100 0	45	100 0	46	100 0	24	100 0

On the basis of the number of probands and controls who had symptoms in *each age group Table 8 shows in the age group* 20—29 *years a slightly higher frequency of lumbago as compared to low back insufficiency In the controls it is the reverse however Sciatica forms the smallest group among the probands* and the controls

In the age group 30—39 years *the number of probands with lumbago was* the highest the presence of sciatica was *lower and lumbar spine insufficiency* occurred least Controls with symptoms on the other hand *had lumbar spine* insufficiency in 60 per cent and lumbago in 40 *per cent No control had* sciatica in this group At the ages between 40—49 years *the same phenomenon* was found among the probands as in the above *mentioned group* while the controls now had a greater frequency of lumbago *as compared to lumbar spine* insufficiency The differences in probands is *statistically significant for lumbago* as compared with sciatica (X^2=5 25* d f = 1) Sciatica *as compared with lumbar* spine insufficiency resulted in (X^2=5 01* d f = 1) *There was no statistical* significance in the controls

In the age group ranging from 50—59 years lumbago hade the greatest frequency in both probands and controls Sciatica had a lower frequency and *lumbar spine insufficiency seldom occurred The differences* between lumbago and sciatica was statistically significant ($X^2=9\ 45^{***}$ d f = 1) in the probands and ($X^2=19\ 63^{***}$ d f = 1) in the controls

In the ages between 60—69 years *lumbago had the highest frequency* also among the probands followed by a statistically significant lower number of subjects with sciatica ($X^2=7\ 63^{**}$ d f = 1) and lumbar spine insufficiency ($X^2=12\ 35^{***}$ d f = 1) In *the controls* the number *of cases of lumbago and* sciatica was of the same magnitude with a lowest frequency of lumbar spine insufficiency

Summary Among the *different* types of low back pain it was found that *the probands* had the lowest frequency of lumbar spine insufficiency and the controls the lowest frequency of sciatica. Lumbago was predominant both in the probands and the controls There was only a statistically significant difference *between the probands* and the controls in the group of lumbar spine insufficiency with a statistically significant higher number of controls who had symptoms of lumbar spine disorders More female than male controls had sciatica but *on the contrary* lumbago was *found more often* in male than female controls

The age distribution in the three most common types of lumbar spine disease revealed that the youngest subjects more often had lumbar spine insufficiency than lumbago The probands aged between 20 and 29 years had a reduced frequency of lumbar spine insufficiency The same phenomenon was found in the controls in the age group ranging from 30—39 years The frequency of lumbago increased from 50—59 years of age Sciatica began with a low frequency in the young group and increased in the probands up to the age group 30—39 years and in the controls in the age group 40—49 years

The mean age of the probands and the controls who had different types of lumbar spine disorders revealed no statistically significant differences

Consistent Cases of Lumbar Spine Disorders (see Fig 3)

Among the subjects with lumbar spine insufficiency consistent cases were found among the probands amounting to 65 8 per cent and among the controls to 91 1 per cent ($X^2=8\ 11^{**}$ d f = 1) *There was a statistically significant* greater frequency in male than female controls ($X^2=4\ 59^{*}$ d.f = 1)

In the group of *lumbago* a consistent past history was found in 39 8 per cent among the probands and in 81 5 *per cent among the controls* A statistically significant greater frequency occurred among the controls ($X^2=29\ 02^{***}$ d f = 1) Among the probands there were more males than females who had a consistent past history of lumbago ($X^2=6\ 62^{*}$ d f = 1)

In the group of *sciatica* 33.3 per cent of the probands and 48 4 per cent of

the probands in the ages between 50—59 years and for the controls aged 40—49 years Then a marked decrease was found in both groups

Hirsch, Jonsson et Lewin (1968) noted the same phenomenae in their female subjects Due to various selections the series cannot be compared in detail with those of the author

TABLE 8 Frequency of Low Back Disorders within the Different Age Groups

		20—29	30—39	40—49	50—59	60—71
Insufficiency	P	9	4	8	10	7
	%	39 2	17 4	14 3	28 6	18 0
	C	5	9	16	7	8
	%	45 4	60 0	35 5	15 2	32 2
Lumbago	P	11	11	30	39	22
	%	47 8	47 8	53 6	41 4	56 4
	C	4	6	17	30	8
	%	36 4	40 0	37 8	65 2	33 9
Sciatica	P	3	8	18	21	10
	%	13 0	34 8	32 1	30 0	25 6
	C	2	0	12	9	8
	%	18 2	—	26 7	19 6	33 9
Total	P %	23 100 0	23 100 0	56 100 0	70 100 0	39 100 0
	C %	11 100 0	15 100 0	45 100 0	46 100 0	24 100 0

On the basis of the number of probands and controls who had symptoms in each age group Table 8 shows in the age group 20—29 years a slightly higher frequency of lumbago as compared to low back insufficiency In the controls it is the reverse however Sciatica forms the smallest group among the probands and the controls

In the age group 30—39 years the number of probands with lumbago was the highest the presence of sciatica was lower and lumbar spine insufficiency occurred least Controls with symptoms on the other hand had lumbar spine insufficiency in 60 per cent and lumbago in 40 per cent No control had sciatica in this group At the ages between 40—49 years the same phenomenon was found among the probands as in the above mentioned group while the controls now had a greater frequency of lumbago as compared to lumbar spine insufficiency The differences in probands is statistically significant for lumbago as compared with sciatica ($X^2=5\ 25^*$ d f $=1$) Sciatica as compared with lumbar spine insufficiency resulted in ($X^2=5\ 01^*$ d f $=1$) There was no statistical significance in the controls

the controls had a consistent past history of lumbar spine disorders There were statistically significant more male than female controls ($X^2=3\ 89^*$ d.f =1)

Within the three groups of lumbar spine disorders consistent past histories were most common in insufficiencies In sciatica the frequency of consistent cases was the lowest.

The age distribution revealed that consistent cases occurred in a statistically significant greater frequency in the younger subjects (cf Table 2 Appendix) The mean age among those with a consistent past history was 44 92 ± 0 94 years There was no statistically significan difference between males and females There were 21 probands and 47 controls with a consistent past history who had had one attack of lumbar spine disorders On close examination of the probands it was found that five of them had had one attack of sciatica 15 one attack of lumbago and one had had a longstanding period of low back insufficiency Out of the controls with one attack 12 had had insufficiency 24 lumbago and 11 sciat ca. The mean age of the probands was slightly lower than that of the controls and, thus there was no statistically significant difference. Furthermore the mean age of the entire group with one attack was slightly lower than that of those with a consistent past history on the whole, however without any statistically significant difference

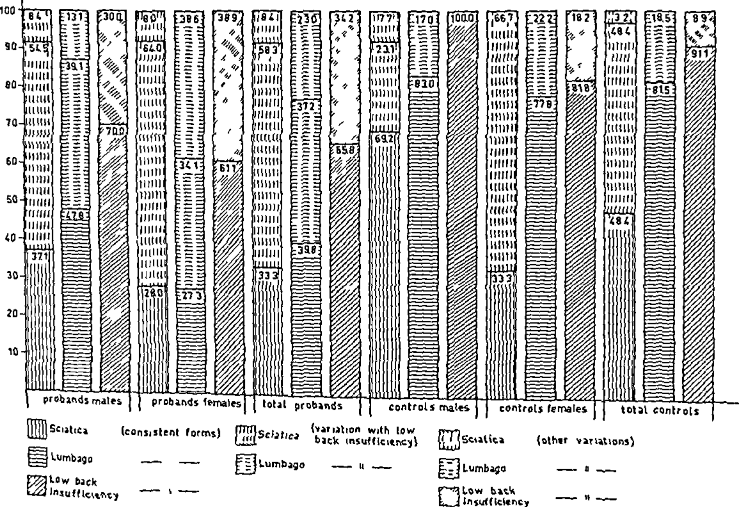
Summary Consistent cases of the three most common types of low back disorders was found more often among controls than probands In consistent cases males with sciat ca and lumbar spine insufficiency predominated among the controls and with lumbago among the probands

The age distribution revealed that the youngest, as a rule, had not experienced more than one attack of low back disorders due to their age

Variation with lumbar spine insufficiency

The most common type of variation is a combination of lumbago and sciatica with low back insufficiency (Fig 3) A variation of sciatica with low back insufficiency was found in 58 3 per cent of the probands, and in 48 4 per cent of the controls A statistically significant higher frequency was found among the female controls as compared to the males ($X^2=5.74^*$ d.f =1) but no statistically significant difference between probands and controls A variation of lumbago with low back insufficiency was found in a statistically significant higher frequency of probands as compared to controls 37 2 per cent against 18.5 per ce t ($X^2=6\ 83^{**}$ d.f =1) There was no difference in the distribution of sex Due to the greater number of subjects with lumbago in the entire series variations of sciatica with low back insufficiency are of approximately the same magnitude as variations of lumbago with low back insufficiency A statistical analysis of the types of lumbar spine syndrome on the other hand, showed a variation with low back insufficiency which was statistically significant more frequent in sciatica than in lumbago ($X^2=14\ 63^{***}$ d f =1)

FIG 3 Consistent Forms and Variation by Different Types of Low Back Disorders



e controls had a consistent past history of lumbar spine disorders. There were statistically significant more male than female controls ($X^2 = 3.89^*$ d.f. = 1)

Within the three groups of lumbar spine disorders consistent past histories were most common in insufficiencies. In sciatica the frequency of consistent cases was the lowest.

The age distribution revealed that consistent cases occurred in a statistically significant greater frequency in the younger subjects (cf. Table 2 Appendix). The mean age among those with a consistent past history was 44.95 ± 0.94 years. There was no statistically significant difference between males and females. There were 21 probands and 47 controls with a consistent past history who had had one attack of lumbar spine disorders. On close examination of the probands it was found that five of them had had one attack of sciatica, 15 one attack of lumbago and one had had a longstanding period of low back insufficiency. Out of the controls with one attack 12 had had insufficiency, 24 lumbago and 11 sciatica. The mean age of the probands was slightly lower than that of the controls and, thus, there was no statistically significant difference. Furthermore, the mean age of the entire group with one attack was slightly lower than that of those with a consistent past history on the whole, however, without any statistically significant difference.

Summary. Consistent cases of the three most common types of low back disorders was found more often among controls than probands. In consistent cases males with sciatica and lumbar spine insufficiency predominated among the controls and with lumbago among the probands.

The age distribution revealed that the youngest, as a rule, had not experienced more than one attack of low back disorders due to their age.

Variation with lumbar spine insufficiency

The most common type of variation is a combination of lumbago and sciatica with low back insufficiency (Fig. 3). A variation of sciatica with low back insufficiency was found in 58.3 per cent of the probands and in 48.4 per cent of the controls. A statistically significant higher frequency was found among the female controls as compared to the males ($X^2 = 5.74^*$ d.f. = 1) but no statistically significant difference between probands and controls. A variation of lumbago with low back insufficiency was found in a statistically significant higher frequency of probands as compared to controls, 37.2 per cent against 18.5 per cent ($X^2 = 6.83^{**}$ d.f. = 1). There was no difference in the distribution of sex. *Due to the greater number of subjects with lumbago in the entire series variations of sciatica with low back insufficiency are of approximately the same magnitude as variations of lumbago with low back insufficiency.* A statistical analysis of the types of lumbar spine syndrome, on the other hand, showed a variation with low back insufficiency which was statistically significant more frequent in sciatica than in lumbago ($X^2 = 14.63^{***}$ d.f. = 1).

The subjects who had variations with low back insufficiency were significantly older (mean age 55 38 ± 0 86 years, t=8 70*** d f =301) than those with a consistent past history Most of them were found in the age group ranging from 50—59 years then the frequency decreased in accordance with the general tendency

The frequency of variations with lumbar spine insufficiency in this series is close to that reported by *Hult* (1964, b)

Variations are more often found among the sick listed than those who are not reported sick, especially in the higher age-groups

Summary Variations with insufficiency have been the cause of most of the recurrences both among probands and controls and appeared in 87 per cent of the subjects complaining of continuous disorders Variations are more common in probands than in controls Variations with insufficiency are more frequent in females

Other types of variation

Other combinations of lumbar disorders occurred more rarely in all the examined groups than variations with low back insufficiency (Fig 3)

Primary sciatica followed by lumbago occurred in one proband (1 7 %) and not in any control Sciatica followed by lumbago and insufficiency occurred in four probands (6 6 %) and in one control (3 2 %)

In the subjects with lumbago there was a variation with sciatica in 11 probands (9 7 %), a variation with sciatica and insufficiency in 15 probands (13 3 %), but in none of the controls The total amounted to 23 per cent

In lumbar spine insufficiency, there was a variation with lumbago in 8 probands (21 2 %) and in three controls (6 7 %) A statistically significant higher frequency of probands as compared to controls with primary insufficiency had variation with lumbago (X^2=7 34** d f =1) In low back insufficiency there was a variation with sciatica in a slightly lower number five probands (13 1 %) and one control (2 2 %) The difference is statistically significant (X =4 83* d f =1)

Similar to lumbago and sciatica varying with insufficiency low back insufficiency with a variation of sciatica had the greatest frequency in the age group 50—59 years On the other hand, these variations were seldom found before the age of 30 years and after the age of 59 years showed a decided decrease

One single proband with sciatica had variations with lumbago On the other hand lumbago as a variation with sciatica occurred much more frequently Variations with insufficiency were found more often both in the group of sciatica and lumbago than variations with merely sciatica and lumbago respectively

Lumbago with a variation of sciatica occurred more frequently in probands than controls (X^2=6 74** d f =1) similar to lumbago with a variation of sciatica and insufficiency (X^2=9 42** d f =1)

A comparatively high number of subjects with low back insufficiency mostly sick listed had variations with lumbago and sciatica This frequency is in accordance with earlier investigations (*Hult*, 1954 b *Hirsch Jonsson et Lewin* 1968)

Summary In the younger age groups consistency cases of low back syndrome are more common and occur either once only or with few recurrences With increasing age the number of recurrences augment often as variations with insufficiency In higher ages almost all the subjects had symptoms of insufficiency irrespective of which type of low back disorders they had at the onset.

5 Age at Onset of Low Back Disorders *(See Fig 4)*

The figure shows at which age the probands and controls, males and females, had their onset of low back disorders 29 probands (13 6 %) 13 of whom were males and 16 females and ten controls (7 1 %) 4 of whom were males and 6 females were subjected to the disease before the age of 20 years

The onset occurred in 44 probands (16 1 %) between 20—29 years of age, 28 of whom were males and 16 females and 47 controls (33 3 %) 30 of whom were males and 17 females

In 56 probands (26 5 %) the onset was stated to be at the ages of 30—39 years 37 males and 19 females and in 41 controls (29 1 %) 24 males and 17 females.

The age at onset in 50 probands (23 6 %) was between 40—49 years 29 of whom were males and 21 females and 24 controls (17 1 %) 14 of whom were males and 10 females

In 27 probands (12 8 %) the age at onset was 50—59 years 15 of whom males and 12 females and in 15 controls (10 6 %) 11 of whom males and 4 females.

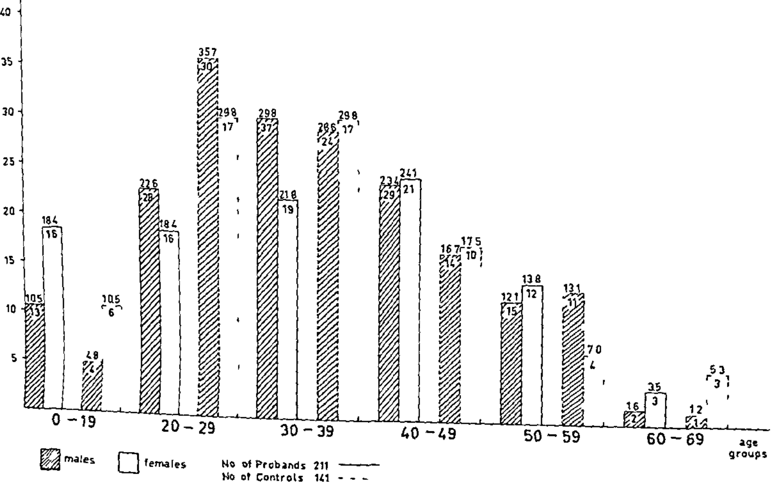
Between the ages of 60—69 years 5 probands (2 4 %) had the onset of low back disorders 2 of whom were males and 3 females and 4 controls (2 8 %) 1 of whom male and 3 females

The mean age of 124 male probands was 35 36 $\pm$ 1 18 years of 87 female probands 34 77 $\pm$ 1 69 years and 84 male controls 34 88 $\pm$ 1 75 years and of 57 female controls 34 12 $\pm$ 1 83 years.

There is no difference between males and females probands and controls Statistically significant differences in the age distribution were found only in the ages 20—29 years at which time a significantly larger number of controls than probands were subjected the first time to low back disorders (χ^2=14 4*** d f =1) The highest frequency of probands (26 5 %) were afflicted with the disease at the age of 30—39 years and the highest frequency of controls (33 3 %) at the age of 20—29 years.

Friberg et Hirsch (1949) found that those who had consulted a physician at hospital for commencing low back disorders were frequently aged between 25—

FIG 4 Age of the Objects at Onset of Low Back Disorders



29 years *Hult* (1954) found the same phenomenon in both his investigations *Unander Scharin* (1950) in his series found that 4 per cent of the cases had the onset before the age of 20 years and 56 per cent at the age of 20—29 years

6 Recurrences

Out of those who had previous symptoms 21 probands (10 %) and 47 controls (33 3 %) had merely one attack of lumbar spine disorders Recurring lumbar spine disorders were found in 190 probands and in 94 controls with a statistically significant higher frequency of the probands ($X^2 = 29\ 64^{***}$ d f = 1) Recurrences occurred according to the following Table

TABLE 9 Recurrences

Two attacks of low back pain	29 probands	6 controls	35
Three	6	8	14
Four	11	2	13
Five	10	5	15
Six " "	8	4	12
Seven " "	3 "	1	4
Eight " " "	2 "	1 "	3
More or persisting "	121 "	67 "	188
Total	190	94	284

Table 9 shows that the majority of both probands and controls had continual low back disorders

Table 10 shows the recurrences according to distribution of sex and age and also the number of probands and controls with recurrences The figures in brackets indicate subjects who had *one* attack of lumbar spine disorders

A higher number of probands had recurrences earlier than the *controls* Already at the age of 29 years 36 4 per cent males and 75 per cent females had recurrences as compared to 25 per cent male and 57 1 per cent female controls

At *the* age of 40 years nearly all the probands had had recurrences while the controls experienced the same 20 years later

It was also found with slight exceptions that with increasing *age the* frequency of recurrences became higher in the series The *mean age of* those who had one attack of low back *disorders is statistically* significant lower than that of those with recurrences, with *the exception* of *female* probands (Table 2 Appendix)

At the time of examination in 1967 it was found that subjects who had been examined and found to have had *one* attack of low back disorders were statis

TABLE 10
Recurrences according to Distribution of Age and Sex

Age	Probands Males	%	Probands Females	%	Controls Males	%	Controls Females	%
20–29	4	36 4 (7)	9	75 0 (3)	1	25 0 (3)	4	57 1 (3)
30–39	13	86 7 (1)	8	100 0 (0)	4	44 4 (5)	4	66 7 (2)
40–49	30	96 8 (1)	25	96 2 (1)	17	65 4 (9)	15	78 9 (4)
50–59	40	93 0 (3)	23	85 2 (4)	15	48 4 (16)	12	80 0 (3)
60–69	24	96 0 (1)	13	100 0 (0)	11	84 6 (2)	11	100 0 (0)
70–	0	– (0)	1	100 0 (0)	0	– (0)	0	– (0)
Total	111	(13)	79	(8)	48	(35)	46	(12)

	Males	Females	Males	Females
Mean age With recurrences	51 03 ±1 01	48 22±1 38	51 45 ± 1 44	49 78 ± 12 06 years
One attack of low back pain	37 31±3 15	42 50±5 26	47 57 ± 1 80	40 83±6 21 years

tically significant free of symptoms more often than those who had had *recurrences* ($X^2 = 20\ 62^{***}$ d f = 1) in probands and ($X^2 = 44\ 33^{***}$ d f = 1) in controls Contrary to this there were statistically significant more probands and controls with symptoms at the time of examination in the group who had had recurrences ($X^2 = 13\ 62^{***}$ d f = 1) and ($X^2 = 52\ 13^{***}$ d f = 1) respectively

Subjects with frequent periods of symptoms were given special attention The cases of recurrences were classified in two groups those with a small number of recurrences and those with eight or more attacks The distribution of age and sex however showed slight differences with a tendency to a higher mean age of those with fewer recurrences except for the female controls where the differences was statistically significant (Table 2 Appendix)

Recurring attacks of low back pain occurred significantly more frequently in probands than in controls The recurrences depended on the age among the controls and increased to 40—49 years among the probands Those who in their early years had had an attack of low back pain stood a greater chance of having recurrences later on Those with low back disorders who were forced to report themselves sick at an early stage consequently risk having more

attacks in the future Not only recurrences were expected but also the number of attacks would depend on the age The investigation revealed that this only happened up to a certain number of recurrences Those who had nine or more attacks of low back disorders were not any older than those with a lower number of recurrences This may be explained by the fact that those who had nine or more attacks of low back disorders had a different type of low back pain viz lumbar spine insufficiency

7 Duration of Symptoms

TABLE 11 Duration of Symptoms

1 week	1—4 weeks	4 weeks—6 months	6 months—1 year	More
P 36 8 %	30 5 %	28 2 %	4 %	0 5 %
C 76 7 *	15 1 %	5 8 %	2 4 %	—

N = 190 Probands and 94 Controls

(X^2 equals duration of symptoms less than one week 36 77*** d f =1 duration of symptoms less than four weeks 18 80*** d f =1)

A statistically significant higher frequency of controls had a short duration of low back disorders on several occasions as compared with the probands

At the first attack the low back disorders lasted for a short time but the difference between the duration of the first attack and the duration of the recurrences was not statistically significant

8 Individual Opinions as to Causes of Symptoms

The subjects were asked to give their opinion on the cause of the onset and the recurrences of low back disorders At the investigation in 1967, 27 9 per cent of the probands and 23 4 per cent of the controls believed that the first symptoms were the result of an accident. 27 4 per cent of the probands and 24 1 per cent of the controls had received symptoms after heavy lifting. True accidents from the legal point of view as a cause of the onset were verified by a higher frequency of probands The difference is not statistically significant Rarely was trauma stated as the cause of recurrences The probands stated trauma in 21 6 pr cent and heavy lifting in 23 2 per cent, the controls mentioned trauma in 10 6 per cent and heavy lifting in 20 2 per cent.

A statistically significant higher frequency of probands than controls had recurrences following an accident (X^2=7 32** d.f =1)

At an attack of low back pain around 1964 the value obtained was (X^2=8 24** d f =1) at the examination in 1967 (X^2=9.31** d.f =1)

TABLE 10

Recurrences according to Distribution of Age and Sex

Age	Probands				Controls			
	Males	%	Females	%	Males		Females	%
20–29	4	36 4 (7)	9	75 0 (3)	1	25 0 (3)	4	57 1 (3)
30–39	13	86 7 (1)	8	100 0 (0)	4	44 4 (5)	4	66 7 (2)
40–49	30	96 8 (1)	25	96 2 (1)	17	65 4 (9)	15	78 9 (4)
50–59	40	93 0 (3)	23	85 2 (4)	15	48 4 (16)	12	80 0 (3)
60–69	24	96 0 (1)	13	100 0 (0)	11	84 6 (2)	11	100 0 (0)
70–	0	– (0)	1	100 0 (0)	0	– (0)	0	– (0)
Total	111	(13)	79	(8)	48	(35)	46	(12)

	Males	Females	Males	Females
Mean age With recurrences	51 03±1 01	48 22±1 38	51 45±1 44	49 78±12 06 years
One attack of low back pain	37 31±3 15	42 50±5 26	47 57±1 80	40 83±6 21 years

tically significant free of symptoms more often than those who had had recurrences (X^2=20 62*** d f =1) *in* probands and (X^2=44 33*** d f =1) *in controls* Contrary to this there were statistically significant more probands and controls with symptoms at the time of examination in the group who had had recurrences (X^2=13 62*** d f =1) and (X^2=52 13*** d f =1) respectively

Subjects with frequent periods of symptoms were given special attention The cases of recurrences were classified in two groups those with a small number of recurrences and those with eight or more attacks The distribution of age and sex however showed slight differences with a tendency to a higher mean age of those with fewer recurrences except for the female controls where the differences was statistically significant (Table 2 Appendix)

Recurring attacks of low back pain occurred significantly more frequently in probands than in controls The recurrences depended on the age among the controls and increased to 40–49 years among the probands Those who in their early years had had an attack of low back pain stood a greater chance of having recurrences later on Those with low back disorders who were forced to report themselves sick at an early stage consequently risk having more

attacks in the future Not only recurrences were expected, but also the number of attacks would depend on the age The investigation revealed that this only happened up to a certain number of recurrences Those who had nine or more attacks of low back disorders were not any older than those with a lower number of recurrences This may be explained by the fact that those who had nine or more attacks of low back disorders had a different type of low back pain viz lumbar spine insufficiency

7 Duration of Symptoms

TABLE 11 Duration of Symptoms

1 week	1—4 weeks	4 weeks—6 months	6 months—1 year	More
P 36 8 %	30 5 %	28 2 %	4 %	0 5 %
C 76 7 %	15 1 %	5 8 %	2 4 %	—

N = 190 Probands and 94 Controls

(χ^2 equals duration of symptoms less than one week 36 77*** d f = 1 duration of symptoms less than four weeks 18 80*** d f = 1)

A statistically significant higher frequency of controls had a short duration of low back disorders on several occasions as compared with the probands

At the first attack the low back disorders lasted for a short time, but the difference between the duration of the first attack and the duration of the recurrences was not statistically significant

8 Individual Opinions as to Causes of Symptoms

The subjects were asked to give their opinion on the cause of the onset and the recurrences of low back disorders At the investigation in 1967 27 9 per cent of the probands and 23 4 per cent of the controls believed that the first symptoms were the result of an accident. 27 4 per cent of the probands and 24 1 per cent of the controls had received symptoms after heavy lifting True accidents from the legal point of view as a cause of the onset were verified by a higher frequency of probands The difference is not statistically significant Rarely was trauma stated as the cause of recurrences The probands stated trauma in 21 6 pr cent and heavy lifting in 23 2 per cent, the controls mentioned trauma in 10 6 per cent and heavy lifting in 20 2 per cent.

A statistically significant higher frequency of probands than controls had recurrences following an accident (χ^2 = 7 32** d.f = 1)

At an attack of low back pain around 1964 the value obtained was (χ^2 = 8.24** d f = 1) at the examination in 1967 (χ^2 = 9 31 * d.f = 1)

A statistically significant higher frequency of controls than probands explained the symptoms occurring spontaneously at the onset ($\chi^2 = 11.36^*$ d f = 4) and at the recurrences ($\chi^2 = 10.40^*$ d f = 4)

A sumptions that low back pain resulting from an accident should be of a more intense kind was not verified in this series A statistically significant higher frequency of controls merely revealed more often intense pain than slight at the onset after an accident ($\chi^2 = 22.45^{***}$ d f = 1) In recurrences there was no difference between probands and controls in this respect For further details see separate Table 5

Pain/ache in the low back due to coughing or sneezing in different diagnoses see separate Table 6

Summary Accidents and heavy lifting interpreted by the subjects as the cause of low back disorders predominated in the probands from the onset and at the recurrences up to the time of examination The differences are difficult to explain by the selection and probably depend on lapse of memory

9 Distribution of Lumbar Spine Diagnoses on Examination in 1967

On the basis of symptoms and signs at the examination in 1967 each proband and control was classified in Diagnostic Groups Belonging to Group 1 were subjects who had no symptoms and no pathological findings of importance In Group 2 were included the subjects who had no symptoms but severe restriction of mobility in the lumbar spine Those classified in Group 3 had symptoms of tiredness weakness sensation of stiffness or dull pain in the lumbar spine radiating feeling of discomfort only if the radiation was not of a radicular kind and previously defined as lumbar spine insufficiency The findings were either quite negative or else there were only insignificant clinical findings such as tenderness on palpation of a spinal process or pain where there was no contraction in the paravertebral musculature either in a recumbent or standing position Group 4 included subjects with lumbago who had severe pain/ache contraction of musculature severe restriction of mobility and tenderness in most of the cases Lasègue s sign was positive Group 5 contained subjects with radiating pain of a radicular kind (sciatica without positive Lasègue s sign and no neurological disturbances) The subjects in Group 6 had sciatica with positive Lasègue s sign but no neurological disturbances In Group 7 the subjects had sciatica with positive Lasègue s sign and neurological disturbances

In Group 1 there were 96 probands and 147 controls The number of controls was statistically significant higher than the number of probands ($\chi^2 = 25.07^{***}$ d f = 1) A statistically significant higher frequency of controls can be explained by the selection and the actual definition of the control group

In Group 2 there were 3 probands and 6 controls all of whom had a high mean age (Table 3 Appendix) with the exception of one female control The

high mean age probably is the explanation of the restricted mobility in the lumbar spine

In Group 3 there were 98 probands and 58 controls A statistically significant greater number of probands was found as compared to controls ($X^2=6\ 99^{**}$ d f =1) A statistically significant higher number of females was found both among the probands and the controls ($X^2=6\ 50^{*}$ d f =1) in probands and ($X^2=6\ 59^{*}$ d f =1) in controls The mean age in Group 3 was similar to that of Group 1

In Group 4 there were only 3 probands None belonged to Group 5 In Group 6 there were 6 probands and in Group 7 there were 6 probands and one female control

Table 12 Examination in 1967 Subjects without and with Symptoms
Without Symptoms (Diagnostic Groups 1—2)

	Probands				Controls			
	Males		Females		Males		Females	
Sciatica	18	51 4	9	36 0	9	69.2	7	38 9
Lumbago	3	53 6	21	47 7	42	89 4	13	72.2
Lumbar spine insufficiency	11	55 0	2	11 1	6	26 1	5	22.7
Earlier free from symptoms	1	100 0	0	–	42	100 0	29	100 0
Total of Subj free from symptoms	67	53 6	32	36 8	99	79.2	54	62.1

With Symptoms (Diagnostic Groups 3—7)

	Probands				Controls			
	Males		Females		Males		Females	
Sciatica	1	43 6	16	64.0	4	30 8	11	61 1
Lumbago	37	46 4	23	5[illegible]3	5	10 6	5	27 8
Lumbar spine insuff	9	45 0	16	88 9	17	73 9	17	77.3
Subj with symptoms	58	46 7	55	63.2	26	20 8	33	37 9
Number of exam. subj	125	100 0	87	100 0	1[illegible]5	100.0	87	100 0

A statistically significant higher frequency of controls than probands explained the symptoms occurring spontaneously at the onset ($X^2=11\ 36^*$ d f =4) and at the recurrences ($X^2=10\ 40^*$ d f =4)

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Pain/ache in the low back due to coughing or sneezing in different diagnoses see separate Table 6

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Table 12 Examination in 1967 Subjects without and with Symptoms

Without Symptoms (Diagnostic Groups 1—2)

	Probands				Controls			
	Males		Females		Males		Females	
Sciatica	18	51.4	9	36.0	9	69.2	7	38.9
Lumbago	37	43.6	21	47.7	42	89.4	13	72.2
Lumbar spine insufficiency	11	55.0	2	11.1	6	26.1	5	22.7
Earlier free from symptoms	1	100.0	0	—	42	100.0	29	100.0
Total of Subj free from symptoms	67	53.6	32	36.8	99	79.2	54	62.1

With Symptoms (Diagnostic Groups 3—7)

	Probands				Controls			
	Males		Females		Males		Females	
Sciatic	17	48.6	16	64.0	4	30.8	11	61.1
Lumbago	32	46.4	23	57.3	5	10.6	5	27.8
Lumbar spine insuff	9	45.0	16	88.9	17	73.9	17	77.3
Subj with symptoms	58	46.7	55	63.2	26	20.8	33	37.9
Number of exam[illegible]	125	100.0	87	100.0	125	100.0	87	100.0

A statistically significant higher frequency of controls than probands explained the symptoms occurring spontaneously at the onset ($X^2=11\ 36^*$ d f =4) and at the recurrences ($X^2=10\ 40^*$ d f =4)

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TABLE 13 History of Pain of Probands and Controls at Various Periods of Lumbar Spine Symptoms

Diagnose Group	Number		Lumbar Spine Symptoms at Onset		Lumbar Spine Symptoms at Recurrence		Lumbar Spine Symptoms around 1964		Lumbar Spine Symptoms on Examin 1967	
	P	C	P	C	P	C	P	C	P	C
1	96	147	95	9	78	38	95	30	—	—
2	3	6	3	3	3	2	3	2	—	—
3	98	58	98	58	94	53	98	58	93	52
4	3	—	3	—	3	—	3	—	3	—
5	—	—	—	—	—	—	—	—	—	—
6	6	—	6	—	6	—	6	—	6	—
	6	1	6	1	6	1	6	1	6	1
Total	212	217	211	141	190	94	211	91	108	56

during a long period of time could be of prognostic value A time analysis concerning the history of pain of the subject from the onset until the examination in 1967 therefore, was carried out

The table shows that 81 3 per cent of the probands without symptoms at the examination (Groups 1—2) had had recurrences while the probands in Group 3 *had had recurrences in 97 9 per cent.* The difference is highly significant (χ^2 = 10 38 * d f = 1)

Out of the controls without symptoms a total of 50 per cent had recurrences and out of 58 controls in Group 3 recurrences occurred in 91 4 per cent. The difference is statistically highly significant (χ^2=30 01*** d f =1)

All the subjects in Groups 4 6 and 7 had recurrences between the onset and up to the time of examination

In order to investigate the pain syndrome of the probands and the controls at the examination and to study any possibilities of analysing the limits between different types of lumbar spine insufficiency Table 14 below was *compiled*

Only 34 probands and 14 controls had earlier had quite symptom free intervals between periods of lumbago or sciatica *Contrary to this* 36 probands and 46 controls had continual spinal symptoms of the insufficiency type 12 probands of whom and one control had variations with sciatica The others either had attacks of slight symptoms occurring merely in connection with strain or slight attacks however without any special stress in the spine The patients were rather vague in their answers, and found it difficult to give exact answers to the

On the basis of previous definitions, the two first groups of diagnoses were combined to involve subjects without symptoms with or without clinical signs The groups of diagnoses 3—7 included subjects with symptoms with or without clinical signs

The subjects without symptoms (Groups 1 and 2) amounted to 46 7 per cent of all the probands and 72 2 per cent of the controls and those with existing symptoms (Groups 3—7) amounted to 53 3 per cent of the probands and 27 8 per cent of the controls (Table 12) There was a statistically significant greater number of probands than controls who at the examination in 1967 had symptoms of lumbar spine disorders ($X^2=25\ 21^{***}$ d f =1)

In 15 probands and one control there was acute lumbago or sciatica ($X^2=38\ 43^{***}$ *d f* =1)

10 Correlation between Various Types of Low Back Disorders and Classification of Diagnoses on Examination in 1967

Table 12 shows the relation between retrospectively interpreted types of low back symptoms and existing symptoms on examination in 1967 47 3 per cent of the probands and controls from the group of sciatica and 63 5 per cent of the group of lumbago were at the time of examination free of symptoms but only 28 9 per cent from the group of insufficiency A statistically significant greater frequency of the subjects with previous lumbago had no symptoms in 1967 as compared to those with sciatica ($X^2=6\ 51^{*}$ d f =1) The statistically significant lowest number of probands and controls without symptoms belonged to the group with low back insufficiency as compared both with sciatica ($X^2=6\ 16^{*}$ d f =1) and lumbago ($X^2=27\ 12^{***}$ d f =1) At the examination there were both among the probands and the controls significantly more males without symptoms as compared to females probands ($X^2=8\ 36^{**}$ d f =1) and controls ($X^2=5\ 31^{*}$ d f =1)

Most of the subjects without symptoms at the time of examination belonged to the group of consistent cases in sciatica 60 5 per cent lumbago 66 4 per cent and insufficiency 85 8 per cent

Summary At the examination in 1967 it was mostly found that subjects in the group of lumbago had no symptoms Those with insufficiency had the most pronounced symptoms The consistent cases of low back disorders more often had no symptoms than those with variations Males were more often than females free of symptoms

History of pain in various groups of lumbar spine diagnosis

The question arose whether the various groups of diagnosis at the investigation in 1967 were classified at random and whether the same series representative

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	P	C	P	C	P	C	P	C	P	C
1	96	147	95	9	78	38	95	30	–	–
2	3	6	3	3	3	2	3	2	–	–
3	98	58	98	58	94	53	98	58	93	55
4	3	–	3	–	3	–	3	–	3	–
5		–	–	–	–	–	–	–	–	–
6	6		6	–	6	–	6	–	6	–
7	6	1	6	1	6	1	6	1	6	1
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1	96	147	95	79	78	38	95	30	—	—
2	3	6	3	3	3	2	3	2	—	—
3	98	58	98	58	94	53	98	58	93	55
4	3	—	3	—	3	—	3	-	3	—
5	—	—	—	—	—	—	—	—	—	—
6	6	—	6	—	6	—	6	—	6	—
7	6	1	6	1	6	1	6	1	6	1
Total	212	212	211	141	190	94	211	91	108	56

during a long period of time could be of prognostic value. A time analysis concerning the history of pain of the subject from the onset until the examination in 1967 therefore was carried out.

The table shows that 81.3 per cent of the probands without symptoms at the examination (Groups 1—2) had had recurrences while the probands in Group 3 had had recurrences in 97.9 per cent. The difference is highly significant (X^2 = 10.38*** d.f. = 1).

Out of the controls without symptoms a total of 50 per cent had recurrences and out of 58 controls in Group 3 recurrences occurred in 91.4 per cent. The difference is statistically highly significant (X^2=30.01*** d.f. = 1).

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Table 4 (cf Table Appendix) shows that the onset of cervical spine symptoms occurs almost simultaneously with the onset of low back disorders but the mean age is slightly higher Thus it can be assumed that the onset of cervical spine disorders as a rule occurs six years later than that of low back disorders The age at onset of thoracic spine disorders is close to that of the lumbar spine, and the difference is not important as regards the mean age (cf Table 5, Appendix)

Wry neck and brachialgia

Wry neck syndrome had occurred before the examination in 1967 in 16 5 per cent of the probands and in 14 2 per cent of the controls Wry neck and brachialgia was found in 30 9 per cent of the probands and 25 4 per cent of the controls mentioned above At the examination in 1967 42 3 per cent of the probands and 37 5 per cent of the controls had brachialgia with cervical spine disorders The high percentage may be explained by the comparatively low number of examined subjects with existing cervical spine disorders

Incidence of thoracic spine syndromes with without radiating pain

Radiating pain in subjects who earlier had thoracic spine symptoms were rarely found Only 9 7 per cent of the probands and 11 3 per cent of the controls with symptoms had stated in their past history that they had had thoracic spine syndrome with radiating pain

Similar to the lumbar spine it proved necessary to differentiate between various types of symptoms also in the cervical and thoracic spine The same definitions as for the lumbar spine namely, intense and slight pain/ache have been employed Insufficiency of the cervical and thoracic spine was defined as a sensation of tiredness weakness stiffness and dull pain assessing the intensity of the pain its duration and relation to the strain Cervical and thoracic spine symptoms were classified in cases with singular attacks with/without radiating pain (thoracic and cervical spine syndrome with/without radiating pain) and in cervical and thoracic spine insufficiency only Table 6 in the Appendix shows that insufficiency occurs more often than singular attacks There was only a statistically significant difference in a combination of cervical and thoracic spine syndrome in the above described types In the probands ($X^2 = 16\,67^{***}$ d f = 1) in the controls ($X^2 = 27\,52^{***}$ d f = 1)

For further details see separate Tables 7—14

12 Correlation between Different Locations of Spinal Pain

Table 6 in the Appendix indicates various types of cervical and thoracic syndromes Some frequencies are too low to allow statistical analysis

Various types of cervical and thoracic spine symptoms mostly occurred in subjects with lumbar spine insufficiency (71 1 % probands and 68 9 % controls 70 4 % of whom were the earlier mentioned probands and 93 5 % were the

TABLE 14 Analysis of Pain Syndrome on Examination in 1967

	P				C				P		C	
	M	%	F	%	M	%	F					%
1 Periods without symptoms	24	41 4	10	18 2	7	27 0	7	21 2	34	30 1	14	23 7
2 Periods with slight symptoms only due to strain	6	10 3	12	21 8	1	3 8	7	21 2	18	15 9	8	13 6
3 Periods with slight symptoms even without strain	16	27 6	9	16 4	10	38 4	9	27 3	25	22 1	19	32 2
4 Persistent Low Back Pain	12	20 7	24	43 6	8	30 8	10	30 3	36	31 9	18	30 5
Total	58	100 0	55	100 0	26	100 0	33	100 0	113	100 0	59	100 0

questions posed The subject s hesitance with respect to the term strain was also remarkable and very diffuse It seems impossible to draw limits between past histories which can serve as a type for further classification of lumbar spine insufficiency

11 Incidence of Cervical and Thoracic Pain

A common idea is that the spine on the whole is a functional unit At the examination in 1967 existing cervical and thoracic spine symptoms therefore, were also given attention It was found that 107 probands (50 5 %) and 81 controls (38 2 %) had had earlier symptoms in the cervical spine The number of probands was significantly higher than that of the controls ($\chi^2 = 5\ 88^*$ d f = 1) 49 probands (23 1 %) and 38 controls (17 9 %) complained of previous *symptoms in the thoracic spine The difference is not statistically significant* Symptoms in both the cervical and thoracic spine were present in 27 probands (12 7 %) and in 24 controls (11 3 %) Out of the above mentioned subjects with cervical spine symptoms 81 probands (75 7 %) and 59 controls (72 6 %) had recurring symptoms 36 probands (73 5 %) and 24 controls (63 2 %) had recurring thoracic spine symptoms

At the time *of examination in 1967 26 probands (12 3 %) and 16 controls (7 5 %) had cervical spine symptoms 7 probands (3 3 %) and 5 controls (2 4 %)* had thoracic spine symptoms There were no statistically significant differences between probands and controls Most of the subjects who were examined had the onset of cervical spine symptoms at the ages ranging from 30—49 years while 6 probands and 5 controls had experienced symptoms before the age of 20 years

Table 4 (cf Table Appendix) shows that the onset of cervical spine symptoms occurs almost simultaneously with the on et of low back disorders but the mean age is slightly higher Thus it can be assumed that the onset of cervical spine disorders as a rule occurs six years later than that of low back disorders The age at onset of thoracic spine disorders is close to that of the lumbar spine and the difference is not important as regards the mean age (cf *Table 5 Appendix*)

Wry neck and brachialgia

Wry neck syndrome had occurred before the examination in 1967 in 16 5 per cent of the probands and in 14 2 per cent of the controls Wry neck and brachialgia was found in 30 9 per cent of the probands and 25 4 per cent of the controls mentioned abo ~ At the examination in 1967 42 3 per cent of the probands and 37 5 per cent of the controls had brachialgia with cervical spine disorders The high percentage may be explained by the comparatively low number of examined subjects *with existing cervical spine disorders*

Incidence of thoracic spine syndromes with without radiating pain

Radiating pain ir subjects who earlier had thoracic spine symptoms were rar ly found Only 9 7 per cent of the probands and 11 3 per cent of the controls with symptoms had *stated in their past history that they had had thoracic spine* syndrome with radiating pain

Similar to the lumbar spine it proved neces ary to differentiate between various types of symptoms also in the cervical and thoracic spine The same definitions as for the lumbar spine namely intense and slight pain/ache have been employed Insufficiency of the cervical and thoracic spine was defined as a sensation of tiredness weakness stiffness and dull pain assessing the in ensity *of the pain its duration and relation to the strain* Cervical and thoracic spine symptoms were classified in cases with singular attacks with/without radiating pain (thoracic and cervical spine syndrome with/without radiating pain) and in cervical and thoracic spine insufficiency only Table 6 in the Appendix shows that insufficiency occurs more often than singular attacks There was only a s at stically significant difference in a combination of cervical and thoracic spine syndrome in the above-descr bed types In the probands ($X^2 = 16\ 67^{***}$ d f = 1) in the controls ($X^2 = 27\ 52^{***}$ d f = 1)

For further details se separate Tables 7—14

12 Correlation between Different Locations of Spinal Pain

Table 6 in the Appendix indicates various types of cervical and *thoracic syn* dromes Some frequencies are too low to allow statistical analysis

Various types of cervical and thoracic spine symptoms mostly occurred in subjects with *lumbar spine insufficiency* (71 1 % probands and 68 9 % controls 70 4 % of whom were the earlier mentioned probands and 93 5 % were the

earlier mentioned controls with cervical and thoracic syndromes of the insufficiency type) A statistically significant higher frequency of the controls had cervical and thoracic symptoms of the insufficiency type (X^2 = 5 43* d f = 1)

Symptoms in the cervical and thoracic spine were found in 56 7 per cent of the probands with sciatica as the initial disease, 64 7 per cent of whom had insufficiency In the control series there was only 32 3 per cent, 80 per cent of whom had insufficiency A statistically significant higher frequency of probands than of controls had symptoms in the cervical and thoracic spine in this group (X^2 = 4 88* d f = 1) Insufficiency was more common among the controls

The probands with lumbago had symptoms in the cervical and thoracic spine in 60 2 per cent 55 9 per cent of whom had insufficiency A statistically significant lower number of controls (35 4 %) had the same combination (X^2=10 15*** d f =1)

Summary Combinations of lumbar spine syndrome with symptoms in the cervical and thoracic spine were commonly found in the group with lumbar spine insufficiency The cases of insufficiency were in the majority in this group Most combinations with cervical and thoracic symptoms occurred among the variations with lumbar spine insufficiency and these groups included the highest frequency of insufficiency of other parts of the spine A lower number of controls had symptoms in the cervical and thoracic spine as compared to the probands On the other hand in the group with sciatica and lumbar spine insufficiency the controls were found to have a comparatively greater frequency of insufficiency in the cervical and thoracic spine than the probands More females than males had symptoms in the cervical and thoracic spine and insufficiency was predominant in the females The differences could however not be statistically analysed due to the low frequency

In order to analyse the subjects from the prognostic point of view they were classified in groups according to which part of the spine the disease had set in Probands with lumbar spine insufficiency and variations in lumbar spine insufficiency more often had cervical and thoracic spine disturbances of the insufficiency type and formed a prognostically demarcated group When probands with lumbar spine insufficiency or variation with lumbar spine insufficiency who had also had cervical or thoracic spine insufficiency were compared with the other probands belonging to the same series the following results were obtained (Table 7 Appendix)

Probands with spine insufficiency had statistically significant more recurrences of lumbar spine symptoms and more often lumbar spine symptoms at the examination in 1967 and also significantly more often symptoms in all three parts of the spine as compared to other probands The mean number of sick listing periods and sick list days was higher in the groups with insufficiency Despite the difference not being statistically significant it is still important due to the fact that the series taken from the National Health Insurance Society only

date from the time after 1955 which is too short a period to allow probands with several recurrences to exhibit significant differences Probands with lumbar spine insufficiency or variations of lumbar spine insufficiency combined with insufficiency symptoms in the cervical or thoracic spine form a significantly inferior group from the prognostic point of view, as compared to the other subjects examined.

Summary of various types of spinal disorders

Lumbago is the most frequently occurring lumbar spine disease Lumbar spine insufficiency was rarely found in the probands and sciatica in the controls There was a statistically significant higher number of controls as compared to probands who had lumbar spine insufficiency of a consistent type It was more common with one attack of lumbar spine symptoms among the controls than among the probands At the examination in 1967 the consistent cases were more often free of symptoms than those who had variations They also had less recurrences On the other hand the probands more often had variations with insufficiency than consistent types of lumbar spine symptoms, a higher frequency of symptoms at the time of examination and more recurrences This phenomenon would explain their reason for consulting a physician with sick listing as a result.

Females more often than males had lumbar spine insufficiency more symptoms from the cervical and thoracic spine and frequently they had symptoms at the time of examination in 1967 The combination of lumbar spine disorders with cervical and thoracic spine syndrome was more often found in the probands with the exception of the group with lumbar spine insufficiency in which the controls more often had symptoms of insufficiency in the cervical and thoracic spine The probands who besides lumbar spine insufficiency or variations with lumbar spine insufficiency also had symptoms of insufficiency in the cervical or thoracic spine had a statistically significant higher rate of recurrences as a rule, persisting symptoms also at the time of examination in 1967 The number of sick days and sick periods was higher than for the other probands

In the young age-groups lumbar spine insufficiency was most common Later lumbago set in and became predominant while sciatica developed later still and progressed with increasing age up to 59 years The youngest subjects in the series were those who had one attack of lumbar spine disorders followed by those with consistent types Variations of lumbar spine disorders were most common in the highest age groups

13 Clinical Findings at Examination

Configuration of the spine

Table 8 in the Appendix shows the clinical charges of configuration in the cervical thoracic and lumbar spine Normal cervical spine was found in 99 5

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per cent Normal thoracic spine was noted in 71 7 per cent of the probands and 73 6 per cent of the controls In the lumbar spine the corresponding figures were 73 6 per cent in the probands and 75 per cent in the controls Slightly more normal thoracic spines were found in the controls who previously had not had symptoms in the lumbar spine as compared to those with earlier symptoms

Scoliosis of the thoracic spine was noted in 9 4 per cent of the probands and 9 8 per cent of the controls and of the lumbar spine in 8 per cent of the probands and 8 9 per cent of the controls No differences were observed between those with earlier lumbar spine syndrome and those without previous symptoms Nor were there any differences between those who at the examination were free of symptoms and those who had symptoms Consequently in this series changes of configuration cannot be regarded as the cause of spinal disorders of the type to which this investigation refers

Painful palpation over spinal process

Table 9 in the Appendix shows the rate of painful palpation over the spinal process in different parts of the spine Painful palpation refers to percussive tenderness with superficial or deep pain in one or several vertebrae and not in the musculature This phenomenon was not often found It was more common in the cervical spine, but rare in the spinal processes of the thoracic vertebrae In the cervical- and lumbar spine the symptom was observed statistically significant more often in the probands than in the controls (X^2 = 11 4*** d f = 1) for lumbar spine and (X^2 = 9 63** d f = 1) for cervical spine The frequency was low and without significant differences in the thoracic spine There was a greater number of probands with lumbar spine symptoms who had percussive tenderness in the cervical spine as compared to those who had no symptoms at the examination (X^2 = 9 81** d f = 1)

Besides differences between the probands and the controls who at the examination either were free of symptoms or else had symptoms the controls with earlier symptoms had significantly more often tenderness in the lumbar spinal processes as compared to those without symptoms (X^2 = 4 19* d f = 1) A comparison between probands and controls without and with symptoms revealed (X^2 = 15 74*** d f = 1) and (X^2 = 9 21** d f = 1) respectively

Summary Painful palpation over the spinal process is significantly more common in probands than in controls The same observation was made when subjects with earlier symptoms were compared with those without symptoms and with subjects who had existing lumbar spine disorders Almost the same phenomenon was found with respect to the cervical spine in probands and controls who either had or had not lumbar spine disorders It is plausible that the onset of cervical spine symptoms in subjects with lumbar spine symptoms could point to a non differentiated spinal disease The low frequency of subjects

complaining of tenderness on palpation of the spinal process and the fact that the assessment is subjective demands a certain amount of reservation with regard to the clinical value of this symptom

Function of the spine (Table 10 Appendix)

The series was classified in different spinal groups normal mobility slight fixation severe fixation and stiffness As a criterion on normal function was regarded symmetrical mobility of the spine in different directions without pain or muscular strain as the definition of mobility is difficult to state in degrees varies in different subjects and also depends on their age Slight and severe fixation of the spine could be determined by the author on the basis of deviations from the normal function

Normal mobility of the cervical spine occurred in 74 1 per cent of the probands and in 80 2 per cent of the controls No differences were found between controls with earlier spinal symptoms and those without symptoms

Controls without symptoms at the examination had a statistically significant greater frequency of normal mobility in the cervical spine as compared to the controls with lumbar spine syndrome (X^2 = 10 21*** d f = 1)

The mobility of the thoracic spine in 99 per cent of the controls and in 98 6 per cent of the probands was normal and the same figures applied to the other groups without any statistically significant difference being noted

In the lumbar spine there was normal mobility in 81 6 per cent of the probands and in 95 8 per cent of the controls The difference is statistically significant (X^2 = 21 14*** d f = 1) and can be explained by a greater frequency of slight fixation of the lumbar spine in the group of probands As has earlier been pointed out in the analysis of Group 2 the difference is found in the higher mean age of probands with a stiffer lumbar spine Slight fixation of the lumbar spine was found in a significantly greater number of subjects who had symptoms at the examination in 1967 as compared to those without symptoms The probands thus had (X^2 = 22 04*** d f = 1) and the controls (X^2 = 8 32** d f = 1) Severe fixation of the lumbar spine occurred to a greater extent at the examination of probands with symptoms (5 3 %) than of those without symptoms (3 %) and in one of the controls with symptoms (1 7 %) Stiff lumbar spine was found in two probands with symptoms at the examination (1 8 %)

Summary Reduced mobility in the lumbar spine at the examination in 1967 was found more frequently in probands than in controls The differences no doubt depended on the age but may also have been caused by a greater frequency of lumbago and sciatica among the probands in 1967 In the controls *who had* lumbar spine syndrome at the time of examination there was a significantly greater frequency of slightly reduced mobility *in the cervical* spine.

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higher in the probands Lasègue's sign ($X^2 = 15.47^{***}$ d.f. = 2) and S.L.R. straining ($X^2 = 27.65^{***}$ d.f. = 2). No controls who were symptom free either previously or at the examination in 1967 had positive Lasègue's sign or S.L.R. straining.

Neurological findings

Table 13 in the *Appendix* shows the most common neurological symptoms as found in the series. In 6 probands and in one control neurological disturbances could be connected with existing spinal disorders. Three probands and two controls had persisting neurological symptoms remaining from sciatica, previously treated with surgery and 17 probands and 5 controls had sciatica remaining from earlier conservative treatment. Two probands and two controls had neurological symptoms due to other reasons (polio, MS). Various types of neurological disturbances occurred in a statistically significant greater frequency among the probands as compared to the controls ($X^2 = 11.53^{*}$ d.f. = 4). The former also had sciatica more often both before and at the examination in 1967. In the controls who previously had no symptoms only one case had neurological disturbances, one had a slight knee jerk on the left side. In those with earlier symptoms there were different types of neurological disturbances in a considerably greater amount according to Table 13 in the Appendix. Neurological disturbances were found in fewer of the cases who had no symptoms on examination in 1967 as compared to those who on the same occasion had symptoms. The difference, however, was not statistically significant.

Summary. Neurological disturbances are significantly more common in probands than in controls as well as in those with earlier symptoms as compared to controls without symptoms. The difference depends on more cases of sciatica in the probands both before and at the examination in 1967. The operative and conservative treatments of sciatica were compared. Past histories in which paresthesia and paresis had been stated were compared with neurological disturbances at the examination. There was no difference between those treated surgically and conservatively.

Neurological disturbances in the upper extremities

Lasègue's mechanism (straight leg raising test) and etiology in the lower extremities have been subject to discussion in the literature and are also well defined (*Lasègue* 1864, *de Beuermann* 1884, *Schober* 1940, *Hohmann, Hackenbroch et Lindemann* 1957, *Turek* 1959, *Adams* 1964). An endeavour has been made to find a similar phenomenon in the upper extremities, and has then been called a stretch test (Dehnungschmerz, *Hohmann, Hackenbrock et Lindemann* 1957). However it is less well defined and is no doubt of less clinical value. Stretch test is regarded as positive if there is radiating pain in the shoulder region on abduction and backward movement of the arm.

Pain on mobility test of spine

Table 11 in the Appendix shows the reaction of pain in various parts of the spine both in extreme movements and in movements on the whole Extreme movements included maximal active movement of the spine In 86 8 per cent, the probands could move their cervical spine without pain and the same applied to the controls in 88 7 per cent There was no difference in the control group with or without earlier lumbar spine syndrome Pain on mobility test of the cervical spine was significantly more often found in the controls who at the time of examination in 1967 had lumbar spine symptoms as compared to those without symptoms (X^2 = 6 62** d f = 1)

The frequency of pain on mobility of the thoracic spine was very low, and there were no statistically significant differences between the probands and the controls or between the groups who before or at the examination in 1967, either had or had not lumbar spine syndrome

Pain on mobility of the lumbar spine occurred in 25 9 per cent of the probands, and in 6 1 per cent of the controls The difference was statistically significant (X = 24 12*** d f = 1), and was caused by the greater number of probands who at the examination in 1967 were included in the Diagnostic Groups 4, 6 and 7 At the examination in 1967, 19 probands (16 8 %) had pain when testing the mobility of the spine and 34 (30 1 %) in connection with extreme movements Contrary to this, only one control (1 7 %) had pain when testing the mobility of the spine and 5 (8 5 %) with extreme movements

The difference between the subjects who at the examination either had no symptoms or symptoms is natural for the probands (X^2 = 52 25*** d f = 1) and for the controls (X^2 = 9 21** d f = 1)

Subjects with earlier lumbar spine disorders did not reveal any statistically significant greater frequency of pain on mobility as compared to those who had no symptoms

Summary Pain on mobility of the spine occurred significantly more often in the probands and the controls who had lumbar spine disorders at the time of examination in 1967 than those who had no symptoms and also more often in probands than controls This depended on the higher frequency of existing lumbago and sciatica in the probands at the examination in 1967

Lasegue s sign (Straight Leg Raising Test)

Positive Lasègue s sign was found according to Table 12 in the Appendix in a total of 15 probands and one control In 7 of the probands Lasègue s sign was positive bilaterally and the same applied to the singular control

Positive Lasegue s sign is included in the definition of the Diagnostic Groups 4 6 and 7 Due to an increased number of cases of lumbago and sciatica in the group of probands, Lasègue s sign and S L R straining were also significantly

14 Roentgen Examination

*After excluding seven pregnant females six males and four females who re*fused to be roentgenologically examined and who were excluded at the matching 195 probands and matched controls could be *examined Out of these* 119 were males and 76 females This constitutes 92 per cent of the 212 subjects who were clinically examined

TABLE 15 Various Ages of Subjects Examined

Age	Males	Females
20—29	10 (—1)	7 (—5)
30—39	15	5 (—3)
40—49	29 (—2)	24 (—2)
50—59	41 (—2)	26 (—1)
60—69	24 (—1)	13
70—		1
Total	119 (—6)	76 (—11)

MEAN AGE

Males 49.54 ± 1.09 years

Females 49.67 ± 1.33 years

Despite the non response of six males and eleven females there was no difference in age between the entire clinical and the roentgenologically *examined subjects* In this series roentgen examination was performed of the thoracic and the lumbar spine using the routine technique of Roentgen Diagnostic Department I, Sahlgrenska sjukhuset Gothenburg The examination was carried out with the patient in a recumbent position with one AP and one lateral projection of the thoracic spine The same projections were used for the lumbar spine with an additional AP and lateral projection for the lumbo-sacral and sacroiliac joint Roentgen of the cervical spine was excluded as the extra work included in obtaining an advantageous result would have been too time-*consuming* for the *Department* In order to obtain a further analysis the controls were classified in groups with those who had had earlier lumbar spine disorders (132 *examined subjects* mean age 51.19 ± 1.67 years) and those without *previous* symptoms (63 roentgenologically examined subjects mean age 48.76 ± 0.96 *years) Those* with symptoms were slightly *older* but not statistically *significant. The* probands were also divided into two groups and *matched with the* above mentioned control groups Furthermore, the *subjects* were classified with respect to lumbar spine disorders at the time of examination

Disc degeneration and spondylosis were defined roentgenologically *in the* following way

The "stretch test" was positive in 15 probands and 10 controls at the examination Reduced reflexions in the upper extremities were noted in two controls One control had reduced sensibility For further details see separate table No 15

Orthopaedic changes in lower extremities

Lowered Pelvis more than 1—2 cm, was found in 12 probands and 9 controls There was no difference between those without and with symptoms

Reduced mobility in the right hip joint occurred in three probands and six controls, in the left hip joint in five probands and seven controls Reduced mobility in the knee and foot joints occurred in 12 probands and 9 controls Deformities of feet and toes were observed in 24 probands and 59 controls other deformities could be noted in the lower extremities in 13 probands and 22 controls

There were no statistically significant differences in the shape of the extremities and the pelvis when comparing between probands and controls with or without symptoms at the examination in 1967 Nor were there any deviations between the controls who had or who had not had previous lumbar spine syndrome For further details see separate table

Summary of objective findings on examination in 1967

The clinical examination of probands and controls resulted as follows

Configurative changes in the spine did not reveal earlier or existing spinal disorders Painful palpation over the spinal process occurred more often in probands than in controls both with earlier and existing symptoms at the time of examination in 1967 as compared to those without symptoms The method, however cannot be regarded as objectively reliable due to the subjectivity which is involved both from the point of view of the physician and the subject The function of the spine and the pain reaction in connection with mobility caused significant differences only between the probands and the controls who on examination had symptoms and no symptoms respectively More cases of positive Lasègue s sign depended on more cases of sciatica among the probands This also applied to neurological disturbances in the lower extremities The occurrence of neurological disturbances afforded satisfactory information as to the presence of earlier sciatica both in operated and non operated cases There was no correlation between a lowered pelvis of more than 1—2 cm and changes in the lower extremities and lumbar spine disorders Neurological disturbances in the upper extremities rarely occurred according to the experience as mentioned in the literature (*Hult* 1954 a b *Adams* 1964 *Hirsch* 1966)

Satisfactory information as to the subject s existing spinal disorders will be obtained on objective examination If there are no neurological disturbances present it is impossible to state definitely earlier occurrence of lumbar spine disorders

14 Roentgen Examination

After excluding seven pregnant females six males and four females who refused to be roentgenologically examined and who were excluded at the matching 195 probands and matched controls could be examined Out of these 119 were males and 76 females This constitutes 92 per cent of the 212 subjects who were clinically examined.

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The stretch test" was positive in 15 probands and 10 controls at the examination Reduced reflexions in the upper extremities were noted in two controls One control had reduced sensibility For further details see separate table No 15

Orthopaedic changes in lower extremities

Lowered Pelvis more than 1—2 cm was found in 12 probands and 9 controls There was no difference between those without and with symptoms

Reduced mobility in the right hip joint occurred in three probands and six controls in the left hip joint in five probands and seven controls Reduced mobility in the knee and foot joints occurred in 12 probands and 9 controls Deformities of feet and toes were observed in 24 probands and 59 controls, other deformities could be noted in the lower extremities in 13 probands and 22 controls

There were no statistically significant differences in the shape of the extremities and the pelvis when comparing between probands and controls with or without symptoms at the examination in 1967 Nor were there any deviations between the controls who had or who had not had previous lumbar spine syndrome For further details see separate table

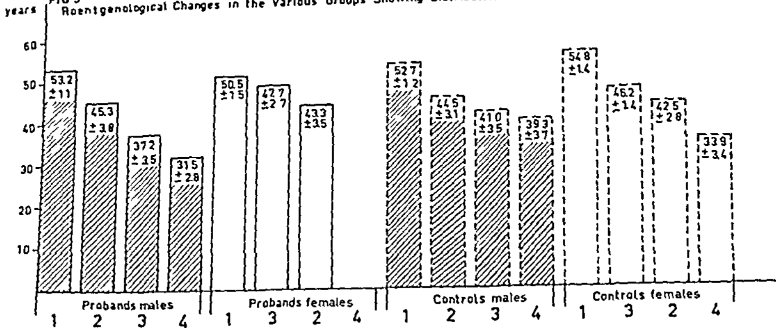
Summary of objective findings on examination in 1967

The clinical examination of probands and controls resulted as follows

Configurative changes in the spine did not reveal earlier or existing spinal disorders Painful palpation over the spinal process occurred more often in probands than in controls both with earlier and existing symptoms at the time of examination in 1967 as compared to those without symptoms The method however cannot be regarded as objectively reliable due to the subjectivity which is involved both from the point of view of the physician and the subject The function of the spine and the pain reaction in connection with mobility caused significant differences only between the probands and the controls who on examination had symptoms and no symptoms respectively More cases of positive Lasègue s sign depended on more cases of sciatica among the probands This also applied to neurological disturbances in the lower extremities The occurrence of neurological disturbances afforded satisfactory information as to the presence of earlier sciatica both in operated and non operated cases There was no correlation between a lowered pelvis of more than 1—2 cm and changes in the lower extremities and lumbar spine disorders Neurological disturbances in the upper extremities rarely occurred according to the experience as mentioned in the literature (*Hult* 1954 a b *Adams* 1964 *Hirsch* 1966)

Satisfactory information as to the subject s existing spinal disorders will be obtained on objective examination If there are no neurological disturbances present it is impossible to state definitely earlier occurrence of lumbar spine disorders

FIG 5
Roentgenological Changes in the Various Groups Showing Distribution According to Mean Age



1 = Diffuse roentgenological changes in both thoracic and lumbar spine
2 = Roentgenological changes limited to lumbar spine
3 = Roentgenological changes limited to thoracic spine
4 = Without roentgenological changes

Disc degeneration included each reduction of the intervertebral distance as compared to the adjoining intervertebral space As regarded the lumbo sacral disc, normally revealing variations degenerative changes were also required of the surrounding edges of the vertebral body

Spondylosis included each type of bone projecting from the edge of the vertebral body (exostosis) As routine projections do not allow a sure diagnosis of intervertebral joint arthritis no attention was paid to this (*Blom* 1967, and *Scheller* 1967)

The roentgen series were studied to find out the occurrence and localization of the above specified pathological changes in each segment of the thoracic and lumbar spine, configurative changes deviations from the shape of the inter vertebral space, e g Scheuermann s disease Schmorl s noduli osteoporosis Bechterew s disease congenital changes spondylosis and spondylolisthesis, spina bifida block vertebrae and transitional vertebrae Furthermore a specification was made of scoliosis, degenerations of a disc and spondylosis

In this investigation were included the roentgenological findings which occurred in a number of subjects who were suitable for statistical analysis

Roentgenological changes (Tables 14 Appendix)

Roentgenological changes of some kind occurred in 96 9 per cent of the probands and in 90 3 per cent of the controls The changes were localized either in the thoracic or the lumbar spine or both in the thoracic and the lumbar spine There was a statistically significant greater frequency of probands than controls who had roentgenological changes ($\chi^2 = 4\ 44^*$ d f $= 1$)

The difference between the controls who had earlier lumbar spine syndrome and those without previous symptoms is not significant There were no differ ences between those without or with symptoms at the examination in 1967

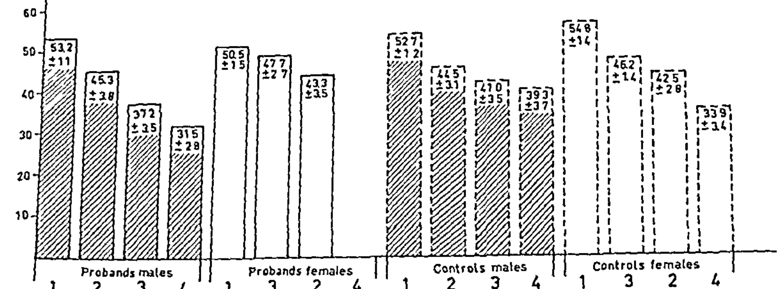
The above mentioned statistically significant differences are found in the group with changes both in the thoracic and the lumbar spine 64 1 per cent of controls and 76 5 per cent of probands

The age and sex distribution showed that the examined subjects who had no roentgenological changes either among the probands or the controls were signif icantly younger than those with roentgenological changes $p(t) < 0\ 05$ The group with changes only in the thoracic or lumbar spine was significantly younger than those with roentgenological changes in both the thoracic and the lumbar spine $p(t) < 0\ 05$ In the ages exceeding 50 years the disc degeneration and changes of spondylosis became more severe and more extended

Roentgenological changes

The roentgenological changes depend on the age In young individuals degen erative disturbances are rarely found but with increasing age they are localized either in the thoracic or the lumbar spine and at the age of 50 years they have a tendency to involve both the thoracic and the lumbar spine

FIG 5.
Roentgenological Changes in the Various Groups Showing Distribution According to Mean Age



1 = Diffuse roentgenological changes in both thoracic and lumbar spine

2 = Roentgenological changes limited to lumbar spine

3 = Roentgenological changes limited to thoracic spine

4 = Without roentgenological changes

Localization of roentgenological changes

A roentgentopographic classification of spinal changes in seven possible combinations according to Table 15 in the Appendix was statistically analysed with consideration taken to all the groups There were no significant differences in any localization between the probands and the controls Nor were there any deviations between controls who had not experienced earlier spinal symptoms and those who had symptoms and matched probands or between those without or with symptoms at the examination

Scoliosis (Table 16, Appendix)

With the roentgen technique used, the existing changes of the configuration depended on the position of the subject on exposure When describing scoliosis the roentgenologist defined it as a spinal curvature in the frontal plane with or without rotation The designations used were plausible, slight, moderate There were three cases of severe scoliosis in the series one proband and two controls All of them had had earlier spinal disorders and stated that they suffered from lumbar spine syndrome also at the time of examination in 1967 This small number does not permit any statistical analysis

Congenital vertebral changes

In the roentgen series there were three types of congenital changes of the vertebrae spina bifida occulta transitional vertebrae and spondylolysis with or without spondylolisthesis

1 *Spina bifida occulta* (Table 17 Appendix)

Spina bifida occulta only occurred in the lumbar spine and in the sacrum of 7 7 per cent of the probands and in 10 8 per cent of the controls There were no statistically significant changes when comparing between the various groups

2 *Transitional vertebrae* (Table 18 Appendix)

In the probands there were 14 8 per cent who had transitional vertebrae Out of these 44 8 per cent were symmetrical 55 2 per cent asymmetrical Out of the probands 46 1 per cent with symmetrical and 56 2 per cent with asymmetrical transitional vertebrae had no symptoms at the examination in 1967 In the controls there were transitional vertebrae in 18 per cent symmetrical in 47 per cent asymmetrical in 52 9 per cent Out of those with symmetrical transitional vertebrae 68 8 per cent of the controls had no symptoms at the examination and the corresponding figure for the asymmetrical subjects was 77 8 per cent A slightly larger number of earlier symptom free individuals had asymmetrical transitional vertebrae The difference however was not statistically significant

3 Spondylolysis with or without spondylolisthesis (Table 19 Appendix)

When studying the series it was found that among the controls who previously had never had symptoms from the lumbar spine there was not one single case of spondylolysis or spondylolisthesis. The difference between the above mentioned group and the controls with spondylolysis and spondylolisthesis respectively who had previously had lumbar spine disorders was statistically significant ($X^2 = 4.77$* d.f. = 1). Spondylolysis and spondylolisthesis occurred more often in the controls with earlier symptoms than in those without earlier lumbar spine disorders. In the spondylolysis and spondylolisthesis series there were more subjects who had not been sick listed for spinal disorders in comparison with the probands. This means that spondylolysis and spondylolisthesis may not seldom cause spinal disorders however to such a slight degree that the subject as a rule does not report himself sick.

Schmorl's noduli (Table 20 Appendix)

Schmorl's noduli in the thoracic and lumbar spine occurred in 12.8 per cent of the probands and in 6.1 per cent of the controls. In the controls without earlier lumbar spine disorders the frequency was 9.5 per cent and in those with earlier symptoms 4.5 per cent. There were no differences between those who were symptom free and those with symptoms at the examination in 1967. Schmorl's noduli therefore cannot be regarded as significant for the earlier or existing spinal disorders of the subjects.

Osteoporosis (Table 21 Appendix)

There were no statistically significant differences when studying the roentgen series. However it must be pointed out that the reliability of the roentgen technique in osteoporosis is dubious. Out of the two subjects who had severe osteoporosis and pathological fractures there was one proband who at the examination had lumbar spine insufficiency. The other was a control who had never had any symptoms.

Disc degeneration (Table 22 Appendix)

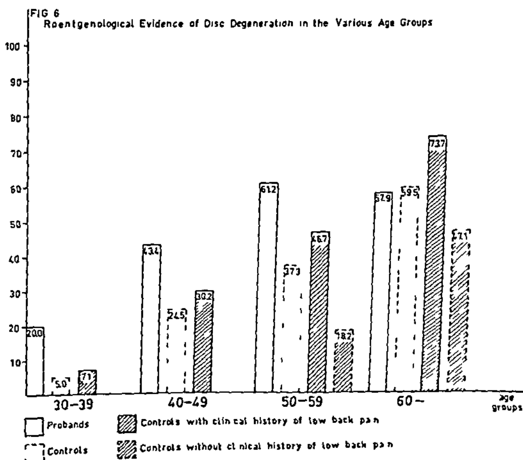
Various degrees of disc degeneration occurred in 46.2 per cent of the probands and in 31.8 per cent of the controls. The number of probands is statistically significant higher than the number of controls ($X^2 = 8.45$** d.f. = 1).

Disc degeneration in controls with lumbar spine disorders was found in 37.2 per cent and in those without earlier lumbar spine disorders in 18.9 per cent ($X^2 = 6.97$* d.f. = 1). A significantly greater number of sick listed and also non sick listed subjects with lumbar spine disorders had disc degeneration as compared to the controls without earlier lumbar spine syndrome. In order to analyse these differences in detail disc degeneration was classified in age and sex (Table 23 Appendix). There were no statistically significant differences

between males and females The mean age in both probands and controls with degenerative changes of a disc was statistically significant higher than the mean age of subjects without changes The difference is about 9 years (Table 23, Appendix) Furthermore in both the control groups those who had degeneration of a disc were of a significantly higher age The difference in age between those who had not had spinal disorders earlier was 7 years, and between those with earlier spinal disorders it was 14 years (Table 23, Appendix)

The occurrence of roentgenologically verified disc degeneration in various age groups is illustrated in Fig 6

The diagram shows how disc degeneration increases with age, advancing in all groups The lowest difference in frequency was found between the probands and the controls with symptoms The highest difference in frequency was observed between the probands and the previously healthy controls When various age groups were statistically analysed it was noted that the above mentioned significant difference between the probands and the controls was only found in the group with moderate disc degeneration on one level, and only in the age group 50—59 years ($X^2=4\ 74^*$ d f =1) (Table 23 Appendix)



There were also differences in ages exceeding 60 years but they were not statistically significant. The difference between the control groups in various types of disc degeneration was significant only above the age of 40 years. There were also severe types of disc degeneration which depended on the age. An interruption of the increasing frequency with advancing ages may be due to the low number of examined subjects included in certain age groups.

Summary. Frequency and degree of disc degeneration increases with advancing age. In those with symptoms, the increase begins earlier and the curve is higher but statistically significant differences occur only in ages exceeding 40 years. The author cannot support *Severin's* (1943) conception. In the series there was a pronounced parallelism between the age and the degree of disc degeneration. Roentgenologically verified disc degeneration did not reveal existing symptoms in the subject. It is plausible that subjects with disc degeneration previously had spinal disorders to a greater extent than those without disc degeneration. Or the reverse: patients with spinal disorders stood a greater chance than healthy subjects to exhibit these kinds of roentgenological changes with increasing age.

Spondylosis (Table 24, Appendix)

Spondylosis in various degrees was found in a large number of the examined subjects: in 84.1 per cent among the probands and in 72.8 per cent among the controls. The difference is statistically significant ($X^2=7.34$** d.f.=1). Severe spondylosis was more common in the probands and contributed to a decided statistically significant difference on one or more levels ($X^2=8.82$** d.f.=1). There were no significant differences between the control groups nor the sex distribution nor the classification of diagnoses at the time of examination in 1967. As in disc degenerations, the occurrence of spondylosis in various age- — and examination groups was followed up.

Similar to disc degeneration, it was found that the subjects who had no spondylosis were statistically significant younger than those with spondylosis. The number of subjects with spondylosis increased with their age, however mostly in those who had been sick listed previously for lumbar spine disorders, slightly less in the non sick listed but with symptoms and least in those without earlier symptoms. The frequency of earlier symptom free controls deviated to a certain extent and was caused by the low number of patients who had been selected at random.

There is a significant difference between the probands and the controls. When the series is classified in age groups, the significant differences are eliminated probably depending on the groups becoming too small (Table 25, Appendix). The degree of spondylosis shows a parallelism with age. Too few patients result in a slight random deviation in severe degrees of spondylosis on one level.

Summary. The phenomenae in spondylosis resemble those of disc degeneration.

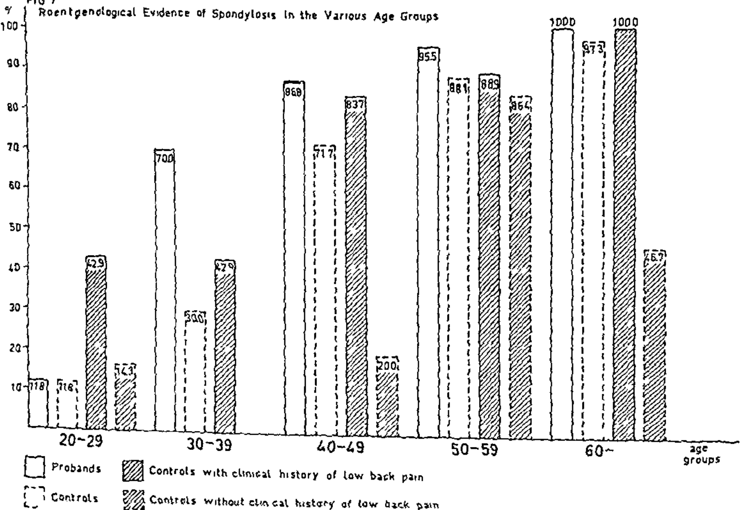


FIG 7
Roentgendological Evidence of Spondylosis in the Various Age Groups

parallelism with age both in quality and quantity The number of cases of spondylosis is however greater in earlier sick listed subjects slightly less in non sick listed, but with symptoms and least in the controls with a previously healthy spine

Summary of roentgenological findings

Roentgenological diagnosis as an indicator of a clinical spinal disease was only applicable to the ages exceeding 40 years for various types of disc degeneration and severe degrees of spondylosis Within the other age groups there was no parallelism It must be pointed out however that moderate disc degeneration on one level may be interpreted differently especially on the L V—S I level

Roentgenologically verified disc degeneration and spondylosis localized to the lumbar or the thoracic spine only become more severe and more extended in ages exceeding 50 years Consequently roentgen examination cannot even in older groups disclose for certain the existing type of disease but may suggest the occurrence of earlier attacks which possibly resulted in sick listing

The frequency of spondylolisthesis and spondylolysis was significantly higher among the controls with previous spinal disease as compared to those who had not had any symptoms and also in comparison with the earlier sick listed probands Symmetrical and asymmetrical transitional vertebrae in previously symptom free subjects were more common than in those with symptoms Therefore transitional vertebrae cannot be regarded as the cause of earlier or existing lumbar spine disorders

15 Discussions and Conclusions

On the basis of the data resulting from this series the problems referred to in the introduction can be answered as follows

1 The past history showed that lumbar spine syndrome had occurred in all the probands except one (who denied any disorders due to lapse of memory) and in 66 5 per cent of the controls (66 4 per cent males and 66 7 per cent females) *Hult* (1954 a b) found incidence of low back pain in 78 per cent industry workers 82 per cent woodsmen 52 7 per cent males with light work and in 64 4 per cent males with heavy labour *Hirsch* (1965 1966) *found that approximately* 65 per cent of the Swedish people some time get lumbar spine disorders

Lumbar spine disorders in young gainfully employed females occurred according to *Hirsch Jonsson et Lewin* (1968) in a lower frequency (49 %) The selection was representative for the female population of this country

The incidence of low back pain in the present control series is in accordance with that stated by most authors. No difference in sex was noted It should be pointed out that the controls are not representative of any statistically significant

uniform group of the population The controls were selected only for the purpo e of being matched with the probands Using the National Health Service Records, it was possible to exclude from the in ended controls, those who had been si k listed during the period 1955—1966 for lumbar spine disorders

Among those with symptoms, lumbago occurred in 53 5 per cent of the probands and 46 1 per cent of the controls Lumbar spine insufficiency was least common among the probands (18 %) and sciatica had the lovest frequency among the controls (22 %) Sciatica occurred among the probands in 28 5 per cent, spinal insufficiency among the controls in 31 9 per cent

There was only a statistically significant difference in the group with lumbar spine insufficiency which had more controls than probands (X^2=**) Differ ences between sex only occurred among the controls, where there were more females than males who had sciatica (X^2=*) and more males than females had lumbago (X^2=***)

Lumbar spine disorders begin early in probands and controls before the age of 20 in 13 6 per cent and 7 1 per cent respectively The number of probands increases between the ages 30—39 years (26 5 %) and of the controls the highest frequencies are reached at the ages between 20—29 years (33 3 %) In the older groups the number decreases both in probands and controls and in the group ranging from 60—69 years only 5 probands (2 4 %) and 4 controls (2 8 %) had their first attack The mean age of probands and controls males and females was close to 35 years and there was no statistically significant difference These findings are very close to those of *Friberg et Hirsch* (1949), *Unander-Scharin* (1950) *Hult* (1954 a) and *Hirsch* (1955)

Lumbar spine insufficiency was mostly present among the youngest subjects and predominated in the age group prior to 29 years and then the frequency decreased A certain increase was observed in the group ranging from 40—49 years in the controls and from 50—59 years in the probands

Lumbago increased with only a few interruptions to the highest agegroups among the probands and to the age group from 50—59 years among the controls

Sciatica only a small percentage occurred among the younger age groups up to between 20—29 years increased among the probands to 35 per cent in the group between 50—59 years and to 39 per cent among the controls in the ages from 40—49 years These results are well in accordance with those observed by *Hult* (1954 a b) and *Hirsch Jonsson et Lewin* (1968)

The frequency of lumbar spine disorders often of the insufficiency type but also lumbago and sciatica occurring at ages under 20 years is higher than that found by *Unander Scharin* (1950) but corresponds to the investigations carried out by the above mentioned authors as well as to the patho anatomical observa tions of disc degeneration reported by *Hirsch et Schajowicz* (1952) and *Hirsch Schajowicz et Galante* (1967)

2 In studying the development of the three most common types of lumbar spine syndrome the series revealed that 42 5 per cent of the probands and 76 6 per cent of the controls only had one and the same type of lumbar spine disorders or only one homogeneous attack of disease so-called consistent cases The frequency of consistent cases among the controls was significantly higher than in the probands and also significantly higher in males than females in both series Variations of different types of lumbar spine disorders occurred in 57 5 per cent of the probands and in 23 4 per cent of the controls with symptoms Contrary to the consistent type variations appeared in a statistically significant greater frequency in probands and females Subjects with consistent symptoms were significantly younger than those with variations The most common types of variation were lumbago and sciatica with lumbar spine insufficiency Variations of lumbago with sciatica and sciatica with lumbago or variations with all the three most common types of lumbar spine disorders were rarely found There was a statistically significant predomination among the probands with variations

Provided that the probands were sick listed due to spinal disorders and generally revealed variations with various types of symptoms it could be assumed that the subjective sensation of the disease was more pronounced than in consistent types in which the controls predominated This opinion is also supported by the fact that among the controls with consistent types of low back pain 43 5 per cent had one single attack of symptoms Consistent cases of lumbar spine insufficiency with the controls predominating was according to these observations no exception from the rule The occurrence of various types of lumbar spine disorders showed that the probands more often than the controls had experienced their symptoms as painful and difficult to endure often appearing in variations On the other hand the controls as a rule had lumbar spine insufficiency and the consistent type This is probably one of the explanations as to why the probands consulted a physician and were sick listed as a result

3 Recurring lumbar spine disorders occurred in 90 per cent of the probands and in 66 7 per cent of the controls with symptoms (X^2 = ***) Recurrence or persisting lumbar spine disorders were also significantly more common among the probands than the controls not infrequently as variations with lumbar spine insufficiency among the probands Recurrence of the initial symptoms occurred earlier and to a greater extent among the probands as compared to the controls At the age of 40 years, nearly all the probands had had a recurrence while among the controls a further 20 years elapsed With increasing age the plausibility of recurrence of lumbar spine disorders augments However the number of recurrences does not only depend on the age Subjects with more than eight recurrences or with persistent symptoms constituted a group in which the age was not higher than in that with a lower frequency of recurrences

At the first attack of lumbar spine disorders the lumbar spine symptoms lasted for a shorter time as compared to most of the recurrences This applied both

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There was only a statistically significant difference in the group with lumbar spine insufficiency which had more controls than probands (X^2=**) Differences between sex only occurred among the controls where there were more females than males who had sciatica (X^2=*) and more males than females had lumbago (X^2=***)

Lumbar spine disorders begin early in probands and controls before the age of 20 in 13 6 per cent and 7 1 per cent respectively The number of probands increases between the ages 30—39 years (26 5 %) and of the controls, the highest frequencies are reached at the ages between 20—29 years (33 3 %) In the older groups the number decreases both in probands and controls and in the group ranging from 60—69 years only 5 probands (2 4 %) and 4 controls (2 8 %) had their first attack The mean age of probands and controls males and females, was close to 35 years and there was no statistically significant difference These findings are very close to those of *Friberg et Hirsch* (1949), *Unander-Scharin* (1950) *Hult* (1954 a) and *Hirsch* (1955)

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within the cervical and lumbar spine This phenomenon was more often found among those with earlier symptoms as compared to those without symptoms The difference was also pronounced when in 1967 subjects with symptoms were put into relation with those who had no symptoms

There were statistically significant differences between the probands and the controls with regard to the function of the spine Significantly more probands than controls deviated one way or the other from the normal pattern of mobility in both the cervical and the lumbar spine (X^2 = ***) or experienced pain at the examination in the cervical and lumbar spine (X^2 = ***) The differences depended on the larger number of probands than controls having symptoms at the examination The mobility test did not result in any retrospective data on spinal disease

Lasègue's sign was positive in a significantly greater number of probands than controls (X^2 = ***) Furthermore there were neurological disturbances significantly more often among the probands than the controls (X^2 = *) The significant deviation was caused by a higher number of probands than controls with existing lumbago-sciatica at the examination in 1967 Neurological disturbances revealed no significant information as to earlier existing sciatica

No significant deviations between the probands and the controls were found when studying the pelvis and the lower extremities and could not be correlated to earlier or existing low pain (*Hult* 1954 b)

In summarizing there were significantly more often objective findings in each proband than in each control the diagnosis being acute lumbago and sciatica (X^2 = ***) Also in the Diagnostic Group 3 either with completely negative or insignificant clinical findings where however subjective symptoms of tiredness weakness stiffness or dull pain in the lumbar spine (lumbar spine insufficiency) was noted the probands predominated significantly as compared to the controls (X^2 = *) The clinical objective findings on examination selected at random corresponded to the existing subjective symptoms of the individual In those who at the examination had symptoms of lumbago or sciatica the objective findings corresponded well In lumbar spine insufficiency there were rarely objective changes in the lumbar spine and the diagnosis was made on the basis of the subject's own description of his symptoms

6 The investigation in 1967 revealed that subjects with lumbar spine syndrome had a significantly greater frequency of restricted mobility than those without symptoms This also applied to the cervical spine and pain experienced at the mobility test of the cervical spine It has been pointed out that the spine is a functional unit and that the cervical and thoracic spine symptoms among subjects with lumbar spine symptoms are pronounced (*Hult* 1954) In the present investigation more than half of the probands and more than 1/3 of the controls had experienced symptoms earlier in the cervical spine Cervical spine symptoms occurred significantly more often among the probands than the

to the probands and the controls A statistically significant higher number of controls had a shorter period of lumbar spine disorders than the probands The probands experienced the recurrences n ore often and earlier than the controls Their disease lasted longer and was often permanent The recurrences give one explanation of the probands tending to report themselves as sick

4 Subjective sensation of pain depends on many various factors and is difficult to assess objectively From the onset until the examination in 1967 the probands on various occasions experienced a statistically significant greater intensity of pain than the controls (χ = **) Significantly more probands than controls felt pain in their lumbar spine day and night (χ^2 = ***) No significantly greater number of controls had lumbar spine symptoms when standing for long periods or when sitting as correlated to a greater frequency of lumbar spine insufficiency among the controls Ischialgia in all the examined cases of low back pain was more frequent among the probands than the controls The deviation, however was significant only when the probands were sick listed in 1964 (X^2 = ***)

All the probands consulted a physician due to low back pain the controls in 51 1 per cent (X^2 = ***) Out of the controls who experienced intense pain/ache in the lumbar spine, 76 7 per cent had consulted a physician which is a statistically significant lower number as compared to the probands (X^2 = ***)

Sensation of intense pain/ache in the spine may be caused by an intense nervous stimulant or a severe change in the spinal segment i e a serious disease Individual differences in sensation of pain/ache may be caused by various degrees of self control, different thresholds of pain and any psychosomatic combinations psycho genous symptoms (*Schanz* 1921, *Weiss et English* 1957, *Rusk* 1958 *Bejerot* 1966 *White* 1966 *Walters* 1966 *Simmons* 1966 *Lindegard* 1967 *Flinchum* 1967 and *Knapp* 1967)

When studying the history of pain on the above mentioned basis a significant frequency of intense sensation of pain in the probands may correspond to a combination of various factors Among the probands painful lumbar spine disorders such as lumbago and sciatica predominated They had recurrences more often and at an earlier stage than the controls more often a variation of lumbar spine syndrome but rarely consistent types The probands furthermore as compared to the controls had ischialgia frequently and not often merely localized pain Again 23 3 per cent more probands than controls had consulted a physician because of intense sensation of lumbar spine symptoms and in slight pain/ache the deviation was 94 per cent

5 At the examination in 1967 no significant differences n the spinal con figuration of the probands and the controls could be noted nor were there any differences between those with earlier symptoms and those without symptoms

Palpation over the spinal process revealed a significantly higher number of probands as compared to controls who complained of deep percussive tenderness

within the cervical and lumbar spine This phenomenon was more often found among those with earlier symptoms as compared to those without symptoms The difference was also pronounced when in 1967 subjects with symptoms were put into relation with those who had no symptoms

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controls (X^2 = *) There was no significant difference on the other hand in thoracic spinal symptoms (23 1 % of probands and 17 9 % of controls) Symp toms from both the cervical and the thoracic spine were present in 12 7 per cent of the probands and in 11 3 per cent of the controls There was no statistically significant deviation Recurrence of cervical spine symptoms among the probands rarely occurred as compared to lumbar spine symptoms (75 7 %) Contrary to *this, the controls more often had recurrences of the cervical spine symptoms* than lumbar spine symptoms (75 6 % of those with symptoms had recurrence in the cervical spine and 66 7 % in the lumbar spine) Almost the same figures applied to the probands with recurrence of thoracic spine symptoms (73 5 %) The controls had the same rate of recurrence of thoracic and lumbar spine symptoms (68 6 %)

At the investigation in 1967 12 3 per cent of the probands and 7 5 per cent *of the controls had cervical spine disorders Thoracic spine symptoms were found* in 3 3 per cent of the probands and 2 4 per cent of the controls No statistically significant deviations were noted between the probands and the controls either with respect to recurrences or symptoms at the examination The onset of cervical spine disorders occurred a few years later than that of lumbar spine syndrome. However, the occurrence of thoracic symptoms following lumbar spine syndrome was only insignificant Out of the probands who before the examination in 1967 had had *cervical spine symptoms 69 1 per cent had had wry neck syndrome* and 30 9 per cent brachialgia Among the controls the frequency of brachialgia was slightly lower (25 4 %) The deviation is not significant Radiating pain in the arms and chest in cases who earlier had thoracic spine syndrome was uncommon only 9 7 per cent of the probands and 11 3 per cent of the controls with symptoms had experienced this

Similar to lumbar spine disorders the pain in the cervical and thoracic spine was experienced in various degree of intensity and duration all depending on the strain of the spine Consequently various types of cervical and thoracic spine syndrome were classified in wry neck and thoracic spine syndrome with/without radiating pain and in existing cervical and thoracic spine insufficiency There was no significant difference between the probands and the controls or between *singular cervical and thoracic spine syndrome A combination of both cervical* and thoracic spine syndrome however occurred significantly more often as cervical and thoracic spine insufficiency than wry neck and thoracic spine syn drome (X^2 = ***) This seems to point to the fact that the spine can be regarded as a functional unit and that there is a correlation between lumbar and cervical spine disorders *and also although less obvious* between lumbar and thoracic spine syndrome The onset and localization of symptoms in all spinal areas the history of pain and also the retrospective distribution of diagnoses were often in accord ance

7 The roentgenological findings were expected to illustrate the differences

between probands sick listed earlier for lumbar spine disorders and their matched non sick listed controls The attention was mainly directed towards congenital changes disc degeneration and spondylosis This was partly done as these diagnoses are most common in a clinical series partly because their importance and clinical relevance are mostly discussed

The present study rarely included other types of roentgenological changes and did not permit statistical analysis Technical errors in connection with the roentgen examination (changes in configuration osteoporosis) furthermore could complicate the analysis of the series

There were three types of congenital changes in the vertebrae spina bifida occulta transitional vertebrae and spondylolysis with or without spondylolisthesis Spina bifida occulta and transitional vertebrae did not differ significantly between the probands and the controls It should be pointed out that a slightly larger number of earlier symptom free controls had asymmetrical transitional vertebrae as compared to symmetrical The number of probands and controls with asymmetrical transitional vertebrae who had no symptoms at the examination in 1967 was identical with all the remaining probands and controls in the series Spondylolysis with or without spondylolisthesis was found in the probands and the controls without any significant deviation There was a statistically significant greater number of subjects with earlier symptoms who had these changes as compared to those without symptoms (X^2 = *)

Hibbs et Swift (1929) *Hodges et Peck* (1937) *Ingebrigtsen* (1937) *Brofeldt* (1937) *Willis* (1941) and *Muralt* (1949) believed that congenital disturbance of the development and especially asymmetrical transitional vertebrae spondylolysis and spondylolisthesis were of great pathological importance for lumbar spine disorders *Willis (1932) Friberg (1939) Hult* (1954 a b) *Hirsch* (1965, 1966) on the contrary do not regard congenital changes of the vertebrae as pathognomonic for spinal disorders A high frequency of congenital changes of the vertebrae, as reported both by *Bistrom* (1954) and *Makowsky* (1963) in subjects with a healthy spine supports the conclusion made by the latter group of authors

Different degrees of disc degeneration occurred statistically significant more often among probands than controls (X^2 = *) more often in subjects with earlier lumbar spine disorders than in those without symptoms (X^2 = *) The analysis and the age distribution however revealed that the difference between the probands and the controls depended on moderate disc degenerations on one level and merely in the age group ranging from 50—59 years (X^2 = *) The difference between those with early symptoms and those without symptoms was caused by various types of disc degeneration however only in those exceeding the age of 40 years Patho-anatomical studies and clinical observations have repeatedly proved that disc degeneration depends on the age of the subject (*Schmorl* 1929 *Friberg* 1941 *Hirsch* 1949 *Hirsch et Schajowicz* 1952 *Hult*

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7 The roentgenological findings were expected to illustrate the differences

subjects in both groups may have similar clinical findings irrespective of the group to which they belonged at the examination in 1967 Retrospective classification of lumbar spine disorders in various groups revealed spinal insufficiency significantly more often among the controls It was also found that with increasing age nearly all the cases of lumbago and sciatica had variations with lumbar spine insufficiency often of a persisting type The predominance in probands with variations of this type was determined at the examination in 1967 in Group 3 *They also had a higher mean age* *Thus these* probands seem to have been sick-listed *due to a more severe type* of spinal disease Spinal insufficiency in subjects who had had *earlier* attacks of lumbago and sciatica seems to be of another type than the true insufficiency which begins in younger subjects *and can be designated* as chronic lumbago The subjective sensation of pain/ache has been dealt with earlier in this chapter It was found that among some of the probands *the subjective sensation* of pain was more intense than among the controls Consistent *types of lumbar spine insufficiency* was found in 11 7 per cent of the probands and 76 *per cent of these had* insufficiency also in the cervical and thoracic spine The corresponding figures for the *controls* were 3 8 per cent and 64 5 per cent respectively Thus there are two groups who objectively reveal the same findings The *logic* explanation of the probands being sick listed seems *to be that* they *experienced* the r subjective symptoms *in a more intense degree*

8 Spinal disorders begin in *comparatively young ages* With *increasing age the* risk *of recurrences becomes greater* Up to about 45 years of age *the recurrences* are mostly of the same character as the initial attack (consistent cases) If the patient experiences intense pain both at the first onset and during the recurrences, *he will* often ask to be sick listed With increasing recurrences the period of sick *listing* becomes longer (Table 16) *)

In the higher ages (mean age 55 38 ± 0 86 years) *the number of* recurrences increased further *and changed* in character Attacks of lumbago *and sciatica* became more uncommon and frequently variations would set in with *lumbar* spine insufficiency The pain was less intense although often of the same character, *the tendency to* report sick became reduced

All *patients aged* up to *70* years as a *rule* only have periods of lumbar spine insufficiency *or permanent* lumbar spine insufficiency *irrespective* of the initial type of lumbar spine disease *These* disorders *due to their* changed character, justify the diagnosis chronic lumbago

*) *NOTE* Table 16 shows the mean figures of the sick list periods and *sick days* of the probands during the *years* 1955—1966 *Unfortunately there are* certain errors. The mean figures are not stated per annum but for the entire period as the *youngest* age groups were not yet included as members of the National *Health* Service and the oldest were already pensioned The table is merely used to illustrate the *prognosis* of the lumbar spine disorders A *detailed* study of the sick listing *problem* and socio-medical connection is being compiled using this series as a basis (*Westrin* 1967—68)

1954 a b, and *Hirsch* 1965 1966) On the basis of the present investigation, th author cannot share *Severin s* (1943) opinion that the intensity of disc degenera tion is independent of age In this series there was a pronounced parallelism between age and the degree of disc degeneration

Early disc degeneration cannot be illustrated on radiograms (*Goldtwait* 1911 *Knutsson* 1944 *Friberg et Hirsch* 1949, *Hirsch* 1951, *Morgan et King* 1957 *Leikkonen* 1959 *Abel et Harmon* 1960 *Wiltberger* 1963, *Lettin* 1967) As the lumbo-sacral disc normally presents large variations in height disc degeneration according to the earlier mentioned definition, was diagnosed at a later stage than discs on other levels

Spondylosis, another type of degenerative changes much resembled disc degen eration Spondylosis in various degrees depending on the age on one or several levels was significant in probands in relation to controls (X^2 = **) There were no differences between the control groups The data in the literature on the subject were very close to those found in this series *Bistrom* (1954) among 151 subjects with a symptom free spine found that spondylosis clearly depended on age *Hodges et Peck* (1937) in their paper mention a greater frequency of spondylarthritis among the controls as compared to the patients a fact which cannot be discussed in this connection as spondylarthritis of varying degrees is not included in the present roentgenological series Similar to *Hult* (1954 a b) the conclusion can be drawn that disc degeneration occurs significantly more often among those with earlier symptoms than among those with a healthy spine Furthermore congenital changes in the vertebrae excepting spondylolisthesis did not cause a higher frequency of low back pain and pretty frequently did spondylolisthesis cause moderate subjective symptoms

Lundberg (1959) concluded his paper with a question which the author consid ered of great importance and to which perhaps there is an answer Which are the factors in rather similar clinical findings that cause one individual to be incapacitated for work and the other to be a capable worker?

The results of the present investigation do not permit any settlement of the question with regard to one singular individual Further it is just as impossible to draw any conclusions in singular cases It is perhaps possible that this series can afford a few viewpoints as to how various population groups accept work

The clinical findings in 1967 on the whole differed significantly between the probands and the controls More probands than controls had reduced mobility and tenderness positive Lasegue s sign and neurological disturbances In 15 probands and in one control only acute lumbago or sciatica was diagnosed at the examination Thus it is obvious that the probands i e those who due to spinal disorders had been incapacitated for work to a statistically significant higher degree than the controls — who carried on working despite spinal disease — had had a decidedly greater attack of spinal symptoms and thus an objectively verified reason to be sick listed On examination selected at random some of the

subjects in both groups may have similar clinical findings irrespective of the group to which they belonged at the examination in 1967. Retrospective classification of lumbar spine disorders in various groups revealed spinal insufficiency significantly more often among the controls. It was also found that with increasing age nearly all the cases of lumbago and sciatica had variations with lumbar spine insufficiency, often of a persisting type. The predominance in probands with variations of this type was determined at the examination in 1967 in Group 3. They also had a higher mean age. Thus these probands seem to have been sick listed due to a more severe type of spinal disease. Spinal insufficiency in subjects who had had earlier attacks of lumbago and sciatica seems to be of another type than the true insufficiency which begins in younger subjects and can be designated as chronic lumbago. The subjective sensation of pain/ache has been dealt with earlier in this chapter. It was found that among some of the probands the subjective sensation of pain was more intense than among the controls. Consistent types of lumbar spine insufficiency was found in 11.7 per cent of the probands and 76 per cent of these had insufficiency also in the cervical and thoracic spine. The corresponding figures for the controls were 31.8 per cent and 64.5 per cent respectively. Thus there are two groups who objectively reveal the same findings. The logic explanation of the probands being sick listed seems to be that they experienced their subjective symptoms in a more intense degree.

8. Spinal disorders begin in comparatively young ages. With increasing age the risk of recurrences becomes greater. Up to about 45 years of age the recurrences are mostly of the same character as the initial attack (consistent cases). If the patient experiences intense pain both at the first onset and during the recurrences he will often ask to be sick listed. With increasing recurrences the period of sick listing becomes longer (Table 16). *)

In the higher ages (mean age 55.38 ± 0.86 years) the number of recurrences increased further and changed in character. Attacks of lumbago and sciatica became more uncommon and frequently variations would set in with lumbar spine insufficiency. The pain was less intense although often of the same character, the tendency to report sick became reduced.

All patients aged up to 70 years as a rule only have periods of lumbar spine insufficiency or permanent lumbar spine insufficiency irrespective of the initial type of lumbar spine disease. These disorders due to their changed character justify the diagnosis chronic lumbago.

*) NOTE. Table 16 shows the mean figures of the sick list periods and sick days of the proband during the years 1955—1966. Unfortunately there are certain errors. The mean figures are not stated per annum but for the entire period as the youngest age groups were not yet included as members of the National Health Service and the oldest were already pensioned. The table is merely used to illustrate the prognosis of the lumbar spine disorder. A detailed study of the sick listing problem and socio-medical connection is being compiled using this series as a basis (West in 1967—68).

TABLE 16 Earlier Sick Listing of Probands

Age Years	Mean + SE of sick list period	Mean + SE of sick list days	Examined Subjects
20—24	1 53 ± 0 19	76 80 ± 34 57	15
25—29	1 75 ± 0 49	118 13 ± 87 15	8
30—34	1 63 ± 0 18	36 50 ± 12 90	8
35—39	2 73 ± 0 42	114 20 ± 31 37	15
40—44	2 50 ± 0 38	136 56 ± 42.78	26
45—49	2 32 ± 0 26	102 90 ± 20 66	31
50—54	2 24 ± 0 34	102 28 ± 23 56	30
55—59	2 58 ± 0 26	117 20 ± 18 10	40
60—64	2 50 ± 0 36	93 45 ± 20 15	19
65—	1 90 ± 0 28	136 85 ± 31 72	20
			Total 212

From the prognostic point of view the subjects should be noted who besides a consistent type of lumbar spine insufficiency or variation with lumbar spine insufficiency had insufficiency disorders also in the cervical or thoracic spine In comparison with the others in this series they had a statistically significant *greater frequency of recurrences, permanent lumbar spine disorders a combination* of disorders in all spinal parts a greater number of sick days and sick listing periods without these differences having any reference to their age

16 Summary

Among all the members of the Gothenburg Social Insurance Office who were sick listed for spinal disorders in 1964 approximately 9 000 members a thirtieth part was selected namely those who were born on the first day of any month For this investigation there were thus 212 probands who were requested to come for examination For earlier- mentioned reasons some failed to appear Thus the total amounted to 76 5 per cent of the probands and 78 8 per cent of the controls The same number of matched controls were selected for the same analysis The matched controls were of the same age sex and belong to the same sickness *benefit category Only Swedish born subjects were examined The controls had* not been reported sick by a physician during the period 1955—1966

The author commenced this investigation by examining the general status of the probands and the controls Then the past history was enquired into including the symptoms in all the spinal parts from the onset until the investigation in 1967 The lumbar and thoracic spine of 195 probands and their matched controls were roentgenologically examined using the routine technique of the Roentgen Diagnostic Department I Sahlgrenska sjukhuset Gothenburg Non response

(six males and eleven females) was caused by pregnancy, refusal to be roentgenologically examined and exclusion of matched pairs as the corresponding subject failed to appear The examination was carried out so as to avoid subjective influence if possible After the examination of the 424 individuals was completed, all the information was transferred to a code system and treated in a data processing machine After tabulating the data various groups and classifications were statistically analysed and the probability calculations were expressed in chi square (X^2) and t test with Degree of Freedom (d.f)

The series thus consisted of 212 probands and the same number of controls out of whom 125 were males and 87 were females The mean age of the males was 49 48 ± 1 07 years and of the females 47 71 ± 1 34 years The age distribution of the probands who were a random sampling of subjects sick listed for lumbar spine disorders revealed that the morbidity of males and females increases to between 50—59 years and the lumbar spine symptoms then rapidly decline The occurrence of lumbar spine disorders both before and at the examination in 1967 wa statistically significant higher in the probands than in the controls

The frequency of lumbar spine disorders was calculated in the control group at 66 5 per cent If the symptoms in all the portions of the spine were included the figure was 81 2 per cent There was no difference in sex and the mean age of those without earlier symptoms did not differ from that of those who had symptoms

The age at the onset of the lumbar spine disorders as stated by the subjects gave the following values mean age of male probands 35 36 ± 1 18 years of female probands 34 77 ± 1 69 years of male controls 34 88 ± 1 75 years and of female probands 34 12 ± 1 83 years

Only one attack of lumbar spine disorders had occurred in 10 per cent of the probands and in 33 3 per cent of the controls with earlier symptoms A statistically significant greater frequency of probands than controls reported recurrence of lumbar spine disorders This also applied to more than eight attacks or permanent symptoms The recurrences depended on the age of the controls and increased to between 40—49 years among the probands The frequency of recurrences increased with age however not among those who had nine or more attacks of lumbar spine disorders Most of the individuals with several recurrences or permanent lumbar spine disorders also had insufficiency in the lumbar region

The first attack of lumbar spine disorders was shorter than most of the recurrences both in the probands and the controls The controls had a shorter duration of lumbar spine disorders than the probands The subjects were asked what in their opinion had cau ed the onset and the recurrences of the lumbar spine syndrome 27 9 per cent of the probands and 23 4 per cent of the controls believed that a cidents were the main cause 27 4 per cent of the probands and 24 1 per cent of the controls mentioned heavy lifting Infrequently trauma and

heavy lifting were stated as the cause of recurrences The differences between the probands and the controls varied statistically significant and the selection could not serve as an explanation

The subjective sensation of pain as experienced by the probands and the controls was using a slightly arbitrary assessment combined to one group, called intense pain/ache, and to another group called slight pain/ache At each examination, significantly more probands than controls complained of intense pain/ache due to lumbar spine disorders No differences in age influenced the pain sensation of the subjects A statistically significant greater number of probands than controls experienced intense pain/ache both at the onset and in connection with most of the recurrences Significantly more probands than controls of those who experienced intense pain/ache or slight pain/ache consulted a physician about their symptoms Even if the history of pain does not serve as a guide when assessing the degree of lumbar spine syndrome it suggests however that the pain more often was experienced as intense by the probands than by the controls and that there was a general tendency to consult a physician

Significantly more probands than controls had pain in the lumbar spine both day and night at all the periods of onset Contrary to this more controls and probands only had symptoms during the day in connection with certain movements or strain This points to the fact that acute and painful lumbar spine disorders more often occurred among the probands than the controls and that lumbar spine insufficiency had a higher frequency in the controls than in the probands

At the onset 28 4 per cent of the probands and 21 9 per cent of the controls had ischialgia The probands (45 %) who in 1964 were sick listed had ischialgia in a significantly higher frequency than the controls (19 8 %)

On the basis of the past history and the first symptoms, the series were classified in three groups of lumbar spine disorders lumbar spine insufficiency lumbago and sciatica The groups were further divided into consistent cases and variations As consistent cases were subjects who from the onset up to the examination in 1967 only had one type of low back pain or merely had a uniform attack of the disease Variations included cases where the pattern of the disease changed e g from sciatica to lumbar spine insufficiency or from lumbago to sciatica Lumbar spine insufficiency and chronic lumbago could seldom be clearly differentiated Consequently a differentiation between the two groups would have been very unreliable Thus the diagnosis chroni lumbago includes lumbar spine insufficiency Pain caused by coaching was not regarded as a spinal disease

Among the described types of lumbar spine disorders lumbago was often found both in the probands and the controls Lumbar spine insufficiency had a statistically significant greater frequency among the controls than the probands Sciatica was rarely found in the controls

There were only significant differences in sex among the controls Significantly

more female controls than males had sciatica but lumbago occurred significantly more often in male than female controls

The age distribution of the subjects with the three most common lumbar spine disorders revealed that the youngest more often had lumbar spine insufficiency and lumbago Already after the age of 20—29 years there was a decline in the probands and one decade later in the controls The frequency of lumbago increased up to 50—59 years Sciatica began with low frequencies in the younger subjects and increased in the probands up to 30—39 years and in the controls up to 40—49 years of age

Consistent cases of the three most common lumbar spine disorders occurred more often among the controls than the probands both males and females Rather often consistent cases were found in the group with lumbar spine insufficiency Consistent cases among those with sciatica were most uncommon The high frequency of lumbago in the series contributed to an increased number of subjects with consistent types of lumbago The most common types of variation were lumbago and sciatica with lumbar spine insufficiency This occurred more often in the probands than in the controls and even more often among females than males The subjects with variations proved to be significantly older than those with consistent symptoms Variations with lumbar spine insufficiency were rather unusual up to the age of 30—39 years after which the frequency increased Variations with insufficiency caused most of the recurrences in both the probands and the controls In this group there were 87 per cent of the subjects who complained only of persisting lumbar spine disorders

Other variations than with lumbar spine insufficiency were uncommon in all the groups The predominance of probands and the number of individuals increasing with age acted in the same way as those who had variation with lumbar spine insufficiency In the higher ages nearly all the probands and controls with symptoms had lumbar spine insufficiency irrespective of which type of disease they had from the beginning

A comparison between different types of lumbar spine disorders in 1967 revealed as a rule that those belonging to the lumbago group were free of symptoms and those belonging to the insufficiency group mostly had symptoms Those with consistent types of lumbar spine disease mostly had no symptoms as compared to those with variations Males had less symptoms than females

The series was subjected to a study of symptoms from the cervical and thoracic spine A significantly higher frequency of probands thans controls had experienced cervical spine symptoms earlier (50 5 % against 39 2 %)

Thoracic spine symptoms occurred rarely in the past history (23 1 % of probands and 17 9 % of controls) 17 7 per cent of the probands and 11 3 per cent of the controls stated that they had suffered from cervical and thoracic symptoms earlier The onset of cervical spine symptoms occurred about six years later than the lumbar spine disorders the thoracic spine disorders mostly began at the

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more female controls than males had sciatica but lumbago occurred significantly more often in male than female controls

The age distribution of the subjects with the three most common lumbar spine disorders revealed that the youngest more often had lumbar spine insufficiency and lumbago Already after the age of 20—29 years there was a decline in the probands and one decade later in the controls The frequency of lumbago increased up to 50—59 years Sciatica began with low frequencies in the younger subjects and increased in the probands up to 30—39 years and in the controls up to 40—49 years of age

Consistent cases of the three most common lumbar spine disorders occurred more often among the controls than the probands both males and females Rather often consistent cases were found in the group with lumbar spine insufficiency Consistent cases among those with sciatica were most uncommon The high frequency of lumbago in the series contributed to an increased number of subjects with consistent types of lumbago The most common types of variation were lumbago and sciatica with lumbar spine insufficiency This occurred more often in the probands than in the controls and even more often among females than males The subjects with variations proved to be significantly older than those with consistent symptoms Variations with lumbar spine insufficiency were rather unusual up to the age of 30—39 years after which the frequency increased Variations with insufficiency caused most of the recurrences in both the probands and the controls In this group there were 87 per cent of the subjects who complained only of persisting lumbar spine disorders

Other variations than with lumbar spine insufficiency were uncommon in all the groups The predominance of probands and the number of individuals increasing with age acted in the same way as those who had variation with lumbar spine insufficiency In the higher ages nearly all the probands and controls with symptoms had lumbar spine insufficiency irrespective of which type of disease they had from the beginning

A comparison between different types of lumbar spine disorders in 1967 revealed as a rule that those belonging to the lumbago group were free of symptoms and those belonging to the insufficiency group mostly had symptoms Those with consistent types of lumbar spine disease mostly had no symptoms as compared to those with variations Males had less symptoms than females

The series was subjected to a study of symptoms from the cervical and thoracic spine A significantly higher frequency of probands thans controls had experienced cervical spine symptoms earlier (50 5 %, against 38 2 %)

Thoracic spine symptoms occurred rarely in the past history (23 1 % of probands and 17 9 % of controls) 12 7 per cent of the probands and 11 3 per cent of the controls stated that they had suffered from cervical and thoracic symptoms earlier The onset of cervical spine symptoms occurred about six years later than the lumbar spine disorders the thoracic spine disorders mostly began at the

same time as the lumbar spine disorders Brachialgia was found in 30 9 per cent of the probands and in 25 4 per cent of the controls with cervical spine symptoms Radiating pain in those with thoracic spine symptoms was found only in 9 7 per cent of the probands and in 11 3 per cent of the controls

Similar to the lumbar spine, symptoms of the insufficiency type also occurred in the cervical and thoracic spine and were defined as a sensation of tiredness weakness stiffness and dull pain with varying degrees of pain duration and depending on strain Longstanding cervical and thoracic spine disorders of the insufficiency type occurred more often than singular acute attacks There was, however only a significant deviation in the combination of cervical and thoracic spine symptoms found both in the probands and the controls

Combinations of various types of symptoms in different portions of the spine mostly occurred in the group with lumbar spine insufficiency and furthermore the number of insufficiency cases in other regions of the spine showed the highest frequency in this group As a rule less controls had symptoms in the cervical and the thoracic spine than the probands Contrary to this the controls belonging to the group with sciatica and lumbar spine insufficiency more often had insufficiency in the cervical and thoracic spine than the probands More females than males had symptoms in the cervical and thoracic spine both with insufficiency types and singular attacks

The probands with lumbar spine insufficiency and variations with lumbar spine insufficiency who also had insufficiency in the cervical or the thoracic spine had a significantly greater number of recurrences of lumbar spine disorders which however were not caused by age A statistically significant greater frequency of lumbar spine disorders at the examination in 1967 with symptoms in all three spinal areas occurred more often as compared to the other probands The mean number of sick listing periods and sick days was also higher in this group than in the other probands

Both among the probands and the controls the variations in the shape of the spine did not illustrate previous or existing spinal symptoms Painful palpation over the spinal process was more often noted in the probands than the controls both among those with earlier symptoms and those with symptoms at the examination However the method is subjective and therefore cannot be regarded as reliable Reduced mobility painful movements and positive Lasègue s sign resulted in significant deviations only in comparison between those without symptoms and those with symptoms at the examination Neurological disturbances revealed not only existing symptoms but also earlier attacks of sciatica There were seldom neurological disturbances in the upper extremities

No correlation was carried out between lowered pelvis >1—2 cm or other changes in the lower extremities and previous or existing lumbar spine disorders found on examination

Roentgenological findings from the lumbar and thoracic spine showed that

disc degeneration and spondylosis depended on age. Changes which in the younger age groups were localized merely to the lumbar or the thoracic spine became aggravated and more extensive in the ages exceeding 50 years Disc degeneration and spondylosis do not confirm the character of the lumbar spine disease but suggest the possibility of earlier attacks which possibly may have resulted in sick listing Of other changes in the vertebrae only spondylolisthesis and spondylolysis occurred in a statistically significant greater frequency among controls with spinal disorders as compared to those without earlier symptoms but also with higher frequencies among the controls than the probands Symmetrical and asymmetrical transitional vertebrae occurred more often among subjects without earlier symptoms than among those with symptoms and, therefore cannot be regarded as the cause of earlier and existing low back pain

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APPENDIX OF TABLES

T ble no I co t

C t t f rm f s tica	1 7 7	1 14	—	2 33 3	4 30 8	2 28 6			6 46 2	2 28 (	5 55 6	2 33 3	2 15 3	2 28 6	2 22.2	2 33 4	—	—	- 2..2	—	13 21	7 23 3	9 12 7	6 15 8
Va tati n w th l b in uffic ney	—	1 6 3			1 5 3			—	3 15 8	4 25 0	—	4 33 3	10 5 6	6 37 5	—	5 41 7	5 26 3	5 31 3	3 100	3 25 0	19 41 3	16 51 6	3 25 0	12 75 0
Va iation with l mbago			—	—	—	—	—	—	—	1 100	—	—		—	—	—		—	—	—	—	1 3 8	—	—
V ri tion with l mbag and insuft	—	—	—	—	—	1 100	—	—	2 66 7	—	1 100	—	1 33 3	—	—	—		—	—	—	3 16 7	1 3 8	1 100	—
Sci tica total	1 2 9	2 8 0	—	2 11 1	5 14 4	3 12 0	—	—	11 31 4	7 28 0	6 46 2	6 33 3	13 37 1	8 32 0	2 15 4	7 38 9	5 14 2	5 20 0	5 38 4	3 16 7	35 28 2	25 .8 7	13 15 7	18 31 0
Consist nt fort s total	11 18 3	9 30 0	4 5 7	6 15 8	11 18 3	5 16 7	9 12 9	6 15 8	21 35 0	8 26 7	22 31 4	13 34 2	12 20 0	7 23 3	30 42 9	7 18 4	5 8 4	1 3 3	5 7 1	6 15 8	60 48 4	30 34 5	70 84 3	38 65 5
Variation with l b i is ff total (only sciatica + lumbago)	—	2 6 5	—	—	1 2 2	—	—	—	4 8 7	12 38 7	3 25 0	4 25 0	26 56 5	10 32 3	1 8 3	7 43 8	15 37 6	7 22 5	8 66 7	5 31 2	46 37 1	31 35 6	12 14 5	16 27 6
Ol er variation total	—	1 3 8	—	1 25 0	3 16 6	3 11 5	—	—	5 .7 8	6 23 1	1 100	2 50 0	5 27 8	10 38 5	—	1 25 0	5 27 8	6 23 1	—	—	18 14 5	26 29 9	1 1 2	4 6 9
Luml ar spine syndromes total	11 8 9	12 13 8	4 4 8	7 12 1	15 12 1	8 9 2	9 10 8	6 10 3	30 24 2	26 29 9	26 31 3	19 32 8	43 34 7	27 31 0	31 37 3	15 25 9	25 20 1	14 16 1	13 15 8	11 18 9	124 100	87 100	83 100	58 100

TABLL NO 1

Fre j ucy of lumbar spine syndromes in different age groups with low back pain history

	20 — 29				30 — 39				40 — 49				50 — 59				60 — 71				20 — 71			
	Prob		Contr		Prob		Contr		Prob		Contr		Prob		Contr		Prob		Contr		Prob		Contr	
	M	I	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Consistent form of l b insuff °	5 35 7	4 36 4	2 8 7	2 11 2	1 7 1	1 9 1	5 21 7	4 22 2	4 28 6	2 18 2	8 34 8	6 33 3	2 14 3	3 27 2	6 26 1	—	2 14 3	1 9 1	2 8 7	6 33 3	14 23 3	11 36 7	23 32 4	18 47 4
Variation with lumbago			—	1 33 3	1 50 0	1 16 7	—	—	—	1 16 7	—	1 33 3	1 50 0	2 33 3	—	1 33 4	—	2 33 3	—	—	2 11 1	6 23 1	—	3 75 0
Variation with sciatica	—	—		—	—	—	—	—	1 25 0	—	—	1 100 0	1 25 0	1 100 0	—	—	2 50 0	—	—	—	4 22 2	1 3 8	—	1 25 0
Low back insuff total	5 25 0	4 22 2	2 8 7	3 13 6	2 10 0	2 11 1	5 21 7	4 18 2	5 25 0	3 16 7	8 34 8	8 36 4	4 20 0	6 33 3	6 26 1	1 4 5	4 20 0	3 16 7	2 8 7	6 27 3	20 16 2	18 20 7	23 27 7	22 38 0
Consistent form of lumbago	5 15 2	4 33 3	2 5 3	2 14 3	6 18 2	2 16 7	4 10 5	2 14 3	11 33 3	4 33 3	9 23 7	5 35 7	8 24 2	2 16 7	22 57 9	5 35 7	3 9 1	0 —	1 2 6	0 —	33 55 0	12 40 0	38 54 9	14 36 8
Variation with l b insufficiency		1 6 7					—	—	1 3 7	8 53 3	3 33 3	—	16 59 3	4 26 7	1 11 1	2 50 0	10 37 0	2 13 3	5 55 6	2 50 0	27 58 7	15 48 4	9 75 0	4 25 0
Variation with sciatica						1 16 7	—	—	2 40 0	1 16 7	—	—	1 20 0	4 66 6	—	—	2 40 0	—	—	—	5 27 8	6 23 1		
Variation with sciatica and insuff		1 9 1	—		2 50 0	—	—	—		3 27 3	—	—	1 25 0	3 27 3	—	—	1 25 0	4 36 4	—	—	4 22 2	11 42 3	—	—
Lumbago total	5 7 2	6 13 6	2 4 3	2 11 1	8 11 (	3 6 8	4 8 5	2 11 1	14 -0 3	1(36 4	12 25 5	5 27 8	26 37 7	13 29 6	23 48 9	7 38 9	16 23 2	6 13 (	6 12 8	2 11 1	19 55 6	44 50 6	47 5(6	18 31 0

TABLE NO 3

D strib u n f d g n t th exa n u n 1967

N nber f d gnoses	I r b nd Mal		P bands Female		Total Pr l and	Control Male		C nt ols I emale		Total Co itrols
	N	M an ge	N	Mean age		N	Mean age	N	Mean ge	
1	64	47 7±1 60	3?	49 0±2 16	96	94	49 3±1 2)	53	47 2±1 57	147
2	3	58 3±6 64	–	–	3	5	61 0±3 98	1	25 0±0	6
3	49	50 3±1 60	49	46 6±1 87	98	26	48 1±3 41	32	48 6±2 40	58
4	2	55 0±0	1	45 0±0	3	–	–	–	–	–
5	–			–	–	–	–	–	–	–
6	3	55 0±0	3	40 0±4 10	6	–	–	–	–	–
7	4	55 0±4 00	2	45 0±0	6	–	–	1	65 0±0	1
I tal	125		87		212	125		87		212

TABLE NO 2

Mean age in relation to number of recurrences

	Without recurrences		With one or more recurrences		
	N	Mean age	N	Mean age	P (t)
Probands Male	13	37 31±3 15 years	111	51 03±1 01 years	<0 05 Stat sign
Probands Female	8	42 50±5 26	79	48 22±1 38	>0 05 Not stat sign
Controls Male	35	47 57±1 80	48	51 45±1 44	<0 05 Stat sign
Controls Female	12	40 83±6 21	46	49 78±1 20	<0 05 Stat sign
	With 1 – 7 recurrences		With more than 7 recurrences or constant low back pain		
	N	*Mean age*	N	*Mean age*	*P (t)*
Probands Male	45	49 67±1 81 years	66	51 97±1 08 years	>0 05 Not stat sign
Probands Female	23	50 65±2 50	56	47 27±1 32	>0 05 Not stat sign
Controls Male	13	55 00±3 75	35	50 14±0 97	>0 05 Not stat sign
Controls Female	13	55 00±2 77	35	47 81±1 18	<0 05 Stat sign

TABLL NO 3

D t b tion of diag o es t th exam n tion 1967

Numbe of d agnoses	P oba d M le		P obands Female		Total Probands	Controls Male		Cont ol Femal		Total Cont ols
	N	Me ag	N	Mean age		N	Mean ag	N	Mean age	
1	64	47 7±1 60	32	49 0±2 16	96	94	49 3±1 29	53	47 2±1 57	147
2	3	58 3±6 64	–	–	3	5	61 0±3 98	1	25 0±0	6
3	49	50 3±1 60	49	46 6±1 87	98	26	48 1±3 41	32	48 6±2 40	58
4	2	55 0±0	1	45 0±0	3	–	–	–	–	–
5	–	–	–	–	–	–	–	–	–	–
6	3	55 0±0	3	40 0±4 10	6	–	–	–	–	–
7	4	55 0±4 00	2	45 0±0	6	–	–	1	65 0±0	1
Tt l	125		87		212	125		87		212

TABLE NO 2

Mean age in relation to number of recurrences

	Without recurrences		With one or more recurrences		
	N	Mean age	N	Mean age	P (t)
Probands Male	13	37 31±3 15 years	111	51 03±1 01 years	<0 05 Stat sign
Probands Female	8	42 50±5 26	79	48 22±1 38	>0 05 Not stat sign
Controls Male	35	47 57±1 80	48	51 45±1 44	<0 05 Stat sign
Controls Female	12	40 83±6 21	46	49 78±1 20	<0 05 Stat sign
	With 1 7 recurrences		**With more than 7 recurrences or constant low back pain**		
	N	Mean age	N	Mean age	P (t)
Probands Male	45	4) 67±1 81 years	66	51 97±1 08 years	>0 05 Not stat sign
Proband Female	23	50 65±2 50	56	47 27±1 32	>0 05 Not stat sign
Controls Male	13	55 00±3 75	35	50 14±0 97	>0 05 Not stat sign
Controls Female	13	55 00±2 77	35	47 81±1 18	<0 05 Stat sign

TABLE NO 6.
Incidence of wry neck and thoracic spine syndromes with without radiation

				Wry neck with without brachialgia	Thoracic spine syndrome with without radiation	Wry neck and thoracic spine syndrome with without radiation	Neck insufficiency	Thoracic spine insufficiency	Cervical and thoracic spine sufficiency	Cervical and thoracic spine disorders	in which insufficiency was found	Total Cervical and thoracic spine disorders	in which insufficiency was found
Previously without symptoms of L.B.P	1 4_ 29	P C	M F M F	1_ _6 10 34 5	1 3 4	1 _4 1 3 4	_ 4 8 1 3.4	1 _4 —	1 2.4 1 3.4	1 40 5 14 48.3	4 23 5 2 14 3	31 43 7	6 19 4
Low Back Insufficiency	20 18 _3 2_	P C	M F M F	_ 10 0 3 16 1 4.3 —	1 5 0 2 11 1 1 4 3 —	— — —	35 0 4 22.2 30 4 6 36 4	_ 10 0 2 11 1 2 8.7 1 4 5	1 5 0 3 16.7 5 21 7 6 _ 3	13 65 0 14 77 8 16 69 6 15 68.2	10 76.9 9 64.3 14 8 .5 15 100 0	27 71 1 31 68 9	19 70 4 29 93 5
Lumbago	69 44 4 18	P C	M F M F	13 18 8 6 13 6 4 8.6 11 1	4 5 8 _ 4 5 — 2 11 1	_9 4 9 1 _ 4.3 1 5 6	11 15 9 9 20.5 3 6 4 1 5 6	2 _9 _ 4 5 3 6 4 1 5 6	10 14.5 3 6.8 1 2.1 3 16.7	4_ 60 5 26 59 0 13 _7 8 10 55 7	2_ 5_4 16 61 5 7 53 8 5 50 0	68 60.2 23 35 4	38 55 9 1_ 5_2
Sciatica	35 _ 13 1	P C	M F M F	6 2_9 3 12.0 — 1 5 6	1 2.9 — 1 [illegible] —	— — — —	6 2_9 6 _4 0 3 _3.1 2 11 1	2 5.7 _ [illegible]0 — 1 5 6	1 2.9 3 1_0 — 2 11 1	20 57.3 14 56 0 4 30 8 6 33.3	11 55 0 11 [illegible]6 3 75 0 5 83.3	34 56.7 10 32.3	2_ 64 7 [illegible] 80.0
Total Proband		_1		3 16.5	10 4 7	6 _8	45 _1.2	1 5.7	_1 9 9	129 60 8	79 61.2		
Total Control		212		30 14._	5 2.4	5 _4	27 1_7	9 4.2	19 8 9	95 44 9	55 57 9		

TABLE NO 4
AGE AT ONSET OF THE WRY NECK/BRACHIALGIA

		Males	Females
0–19 years	P	3	3
	C	2	3
20–29 years	P	8	4
	C	3	3
30–39 years	P	15	9
	C	15	16
40–49 years	P	14	14
	C	10	13
50–59 years	P	14	15
	C	9	7
60–69 years	P	7	1
	C	–	2
70 years	P	–	–
	C	1	–

Mean Age + SE
61 M P = 42 78 ± 1 83
45 F P – 42 50 ± 1 93
40 M C – 40 87 ± 1 55
41 F C = 40 48 + 2 12

Males t – 0 79 d f = 99
Females t – 0 70 d f = 84

TABLE NO 5
AGE AT ONSET OF THORACIC SPINE SYNDROME

		Males	Females
0–19 years	P	3	5
	C	1	3
20–29 years	P	3	2
	C	1	2
30–39 years	P	5	7
	C	6	5
40–49 years	P	6	6
	C	3	6
50–59 years	P	3	7
	C	5	3
60–69 years	P	2	–
	C	1	2
70– years	P	–	–
	C	–	–

Mean Age + SE
22 M P = 38 41 ± 3 46
27 F P = 37 05 ± 3 07
17 M C = 42 35 ± 3 38
21 F C = 39 72 ± 4 15

Males t = 0 81 d f = 37
Females t = 0 51 d f = 44

TABlI NO 6

In dence of wry n k and thoracic p ne synd ome w th without radiat on

				W y n ck w th/ w thout brach l gia	Thor c c spin syndr m w th/ with > t diation	Wry n ck and thora c c spine yndrome w th/ w il out radiati n	Neck insufti c ency	Tho cic spi e in s ft ciency	Cer ic l and thora cic spine sufficl ncy	Cervic l and thora cic spin disord rs	in wh ch in fti ciency was found	Total C rv cal and thora cic pine di orders	in which insufti ciency w fo nd
Previ usly w tho t sy pt ms of L.B P	I	P	M										
			F										
	42	C	M	12 28 6	—	1 2 4	2 4 8	1 2 4	1 2 4	17 40 5	4 23 5	31 43 7	6 19 4
	29		F	10 34 5	1 3 4	1 3 4	1 3 4	—	1 3 4	14 48 3	2 14 3		
Low Back Ins fic ncy	20	P	M	2 10 0	1 5 0	—	7 35 0	2 10 0	1 5 0	13 65 0	10 76 9	27 71 1	19 70 4
	18		F	3 16 7	2 11 1	—	4 22 2	2 11 1	3 16 7	14 77 8	9 64 3		
	23	C	M	1 4 3	1 4 3	—	7 30 4	2 8 7	5 21 7	16 69 6	14 87 5	31 68 9	29 93 5
	22		F	—	—	—	8 36 4	1 4 5	6 27 3	15 68 2	15 100 0		
Lumbago	69	I	M	13 18 8	4 5 8	2 2 9	11 15 9	2 2 9	10 14 5	42 60 5	22 52 4	68 60 2	38 55 9
	44		I	6 13 6	2 4 5	4 9 1	9 20 5	2 4 5	3 6 8	26 59 0	16 61 5		
	47	C	M	4 8 6	—	2 4.3	3 6 4	3 6 4	1 2 1	13 27 8	7 53 8	23 35 4	12 52 2
	18		I	2 11 1	2 11 1	1 5 6	1 5 6	1 5 6	3 16 7	10 55 7	5 50 0		
Sciatica	35	I	M	8 22 9	1 2 9	—	8 2?9	2 5 7	1 2 9	20 57 3	11 55 0	34 56 7	22 64 7
	25		I	3 12 0	—	—	6 24 0	2 8 0	3 12 0	14 56 0	11 78 6		
	13	C	M	—	1 7 7	—	3 23 1	—	—	4 30 8	3 75 0	10 32 3	8 80 0
	18		F	1 5 6	—	—	2 11 1	1 5 6	2 11 1	6 33 3	5 83 3		
Total Proband		212		35 16 5	10 4 7	6 2 8	45 21 2	12 5 7	21 9 9	129 60 8	79 61 ?		
Total Control		212		30 14 2	5 2 4	5 2 4	27 12 7	9 4 2	19 8 9	95 44 9	55 57 9		

TABLE NO 7

Comparison between probands with diffuse insufficiency and other probands

	No of probands	Existing diffuse insufficiency	Mean age and SE	Mean value of recurrences	Existing symptoms in all parts of spine	Lumbar spine syndrome on examination	Mean value of sick reports	Mean value of sicklisting days
Low back insufficiency or variation with low back insufficiency and insufficiency in cervical or thoracic spine	N=64	N=64 Stat sign rarely	Not stat sign 49 72±1 45 years	Stat sign higher 9 42±0 20 (T 9 19+++ d f =209)	N=20 Stat sign frequently (χ^2=23 75+++ d f =1)	N=40 Stat sign frequently (χ^2=21 48+++ d f =1)	Not stat sign 2 30±1 84	Not stat sign 115 23±17 55
Other probands	N=147	N=147 Stat sign frequently (χ^2=65 30+++ d f =1	Not stat sign 47 92±1 07 years	Stat sign lower 6 01±0 31	N=9 Stat sign rarely	N=64 Stat sign rarely	Not stat sign 2 23±0 13	Not stat sign 99 95±10 51

TABLE NO 8
Configuration of the spine

		Cervical spine				Thoracic spine								Lumbar spine							
		Normal		Not normal		Normal		Straight		Increased kyphosis		Scoliosis		Normal		Straight		Increased lordosis		Scoliosis	
Entire series	N = 212P	211	99.5	1	0.5	152	71.7	29	13.7	11	5.2	20	9.4	156	73.6	33	15.6	6	2.8	17	8.0
	N = 212C	211	99.5	1	0.5	150	73.6	19	9.1	16	7.5	21	9.8	159	75.0	29	13.7	5	2.4	19	8.9
Controls without past history of l b p	N 71C	71	100.0			61	85.9	2	2.8	2	2.8	6	8.5	55	77.5	10	14.0	1	1.6	5	6.9
Controls with previous l b p symptoms	N = 141C	140	99.3	1	0.7	95	67.4	17	12.1	14	9.9	15	10.6	104	73.8	19	13.5	4	2.8	14	9.9
Without clinical symptoms of l b p at the examination 1967	N = 99P	99	100.0	–		67	67.7	16	16.2	6	6.1	10	10.0	67	67.7	19	19.2	4	4.0	9	9.1
	N = 153C	153	100.0	–		113	73.9	15	9.8	12	7.9	13	8.4	114	74.5	22	14.4	4	2.6	13	2.5
Clinical symptoms of l b p found at the examination 1967	N = 113P	112	99.1	1	0.9	85	75.2	13	11.5	5	4.4	10	8.9	89	78.8	14	12.4	2	1.8	8	7.0
	N = 59C	58	98.3	1	1.7	43	72.9	4	6.8	4	6.8	8	13.5	45	76.3	7	11.9	1	1.7	6	10.1

TABLE NO 9

Painful palpation over spinal process

Tenderness on palpation

		Cervical spine	%	Thoracic spine	%	Lumbar spine	%
Entire series	N=212 P N=212 C	24 6	11 3 2 8	10 4	4 7 1 9	27 8	12 7 3 8
Controls without past history of l b p	N= 71 C	2	2 8	0	—	0	—
Controls with previous l b p symptoms	N=141 C	4	2 8	4	2 8	8	5 7
Without clinical symptoms of l b p at the examination 1967	N= 99 P N=153 C	4 3	4 0 1 9	2 2	2 0 1 3	3 2	3 0 1 3
Clinical symptoms of l b p found at the examination 1967	N=113 P N= 59 C	20 3	17 7 5 1	8 2	7 1 3 4	24 6	21 2 10 2

TABLE NO 10
Fu ct n f th pi

		Cer cal pi				Th r cic p e				Lu b r p ne			
		N m l	Sl ghtly f d	C sid er bly fix d	Rigid	Normal	Sl ghtly f d	Co sid rably fi d	Rigid	Normal	Sl ghtly fi ed	Co d erably fix d	Rigid
Ent re series	N – 212P N 212C	157 41 170 80 2	41 19 3 32 15 1	14 6 6 10 4 7	— — —	210 99 0 20) 98 6	1 0 5 2 0 9	1 0 5 1 0 5	— — — —	173 81 6 03 95 8	28 13 2 8 3 7	9 4 3 1 0 5	2 0 9 — —
Contr ls with out p st history of l b p	N – 71C	56 8 9	12 16 9	3 4 2	—	70 98 6	1 1 4	— —	— —	68 95 8	3 4 2	— —	— —
C ntrols with pre ious l b p syn ptoms	N 141C	114 80 9	20 14 2	7 4 9	—	139 98 6	1 0 7	1 0 7	— —	135 95 7	5 3 5	1 0 8	— —
Without cl nical sympt m of l b p at the e aminati n 1967	N – 991 N 153C	6 76 8 131 85 6	16 16 2 15 9 8	7 7 0 7 4 6	— — —	98 98 9 151 98 7	— — 2 1 3	1 1 1 — —	— — — —	94 95 0 147 96 1	2 2 0 6 3 9	3 3 0 — —	— — — —
Clin al sym toms f l b p found at the exami ation 1967	N – 1131 N = 59C	81 71 7 39 66 1	25 22 1 17 28 8	7 6 2 3 5 1	— — —	112 99 1 58 98 3	1 0 9 — —	1 1 7	— — — —	79 69 9 50 84 7	2(23 0 8 13 6	6 5 3 1 1 7	2 1 8 — —

TABLE NO 11

Pain on mobility test of spine

		Cervical spine						Thoracic spine						Lumbar spine					
		No pain	%	Pain on extreme movement	%	Pain on movement	%	No pain	%	Pain on extreme movement	%	Pain on movement	%	No pain	%	Pain on extreme movement	%	Pain on movement	%
Entire series	N = 212 P	184	86 8	20	9 4	8	3 8	210	99 1	2	0 9	—	—	157	74 1	36	17 0	19	8 9
	N = 212 C	188	88 7	18	8 5	6	2 8	208	98 1	4	1 9	—	—	199	93 9	7	3 3	6	2 8
Controls without past history of l b p	N – 71 C	62	87 3	9	12 7	—	—	70	98 6	1	1 4	—	—	70	96 6	1	1 4	—	—
Controls with previous l b p symptoms	N = 141 C	126	89 3	9	6 4	6	4 3	138	97 9	3	2 1	—	—	129	91 4	6	4 3	6	4 3
Without clinical symptoms of l b p at the examination 1967	N – 99 P	90	90 9	9	9 1	—	—	99	100 0	—	—	—	—	96	96 9	3	3 1	—	—
	N = 153 C	141	91 9	11	7 1	1	0 7	153	100.0	—	—	—	—	151	98 7	2	1 3	—	—
Clinical symptoms of l b p found at the examination 1967	N – 113 P	95	84 1	11	9 7	7	6 2	109	96 5	4	3 5	—	—	60	53 1	34	30 1	19	16 8
	N = 59C	47	79 7	7	11 9	5	8 5	55	93 2	4	6 8	—	—	53	89 8	5	8 5	1	1 7

TABLE NO 12
Vr ght leg a g t t (La b gn)

		Straight leg raising test right		Straight leg raising test left		SLR tightness right		SLR tightness left	
Entire series	N = 212 I N = 212 C	11 1	5 2 0 5	11 1	5 2 0 5	12 1	5 7 0 5	13 1	6 1 0 5
Controls without past history of l b p	N = 71 C	0	–	0	–	0	–	0	–
Control with previous l b p symptoms	N – 141 C	1	0 7	2	1 4	1	0 7	2	1 4
Without clinical symptoms of l b p at the examination 1967	N = 93 P N = 153 C	0 0	– –	0 0	– –	0 0	– –	0 0	– –
Clinical symptoms of l b p found at the examination 1967	N = 113 P N = 59 C	11 1	9 7 1 7	11 2	9 7 3 4	12 1	10 6 1 7	13 2	11 5 3 4

TABLE NO 11

I ain on mobility test of spine

		Cervical spine						Thoracic spine						Lumbar spine					
		No pain	°o	Pain on ex treme move ment	°	Pain on move ment	%	No pain	°o	Pain on ex treme move ment	/o	Pain on move ment	/o	No pain	°o	Pain on ex treme move ment	%	Pain on move ment	%
Entire series	N = 212 P N = 212 C	184 188	86 8 88 7	20 18	9 4 8 5	8 6	3 8 2 8	210 208	99 1 98 1	2 4	0 9 1 9	– –	– –	157 199	74 1 93 9	36 7	17 0 3 3	19 6	8 9 2 8
Controls without past history of l b p	N = 71 C	62	87 3	9	12 7	–	–	70	98 6	1	1 4	–	–	70	96 6	1	1 4	–	–
Controls with previous l b p symptoms	N = 141 C	126	89 3	9	6 4	6	4 3	138	97 9	3	2 1	–	–	129	91 4	6	4 3	6	4 3
Without clinical symptoms of l b p at the examina tion 1967	N = 99 P N = 153 C	90 141	90 9 91 9	9 11	9 1 7 1	– 1	– 0 7	99 153	100 0 100.0	– –	– –	– –	– –	96 151	96 9 98 7	3 2	3 1 1 3	– –	– –
Clinical symptoms of l b p found at the examina tion 1967	N – 113 P N – 59C	95 47	84 1 79 7	11 7	9 7 11 9	7 5	6 2 8 5	109 55	96 5 93 2	4 4	3 5 6 8	– –	– –	60 53	53 1 89 8	34 5	30 1 8 5	19 1	16 8 1 7

TABLE NO 14 I d xc f R x ge olog cal Ch ng
R entgenol gical f nd s

	I ntire serie				C s with out p st hi tory of l b p		C r spo d ng P s		C s w th p v u l b p syn ptom		Cor e pond ng P s		Cl syn pto ns of l b p at the examination 1967				Without l y np tom of l l p at th e mi t on 1967			
	Probands		Control		Controls		Probands		Controls		Prob n ls		Prol ands		Controls		Prob nds		Cont ol	
0 N n interpretable	0		0	—	0	—	0	—	0	—	0		0	—	0	—	0	—	0	—
1 N change	6	3 1	19	9 7	9	14 3	2	3 2	10	7 6	4	3 0	4	4 3	14	9 9	2	1 9	5	9 3
2 Change limited to thoracic sp ne	13	6 6	14	7 2	6	9 5	6	9 5	8	6 1	7	5 3	6	6 5	10	7 1	7	6 8	4	7 4
3 Chang s l mited to luml ar spine	27	13 8	37	19 0	11	17 5	5	7 9	26	19 7	22	16 7	13	14 1	24	17 0	14	13 6	13	24 1
4 Changes in both thoracic and lumbar pine	149	76 5	125	64 1	37	58 7	50	79 4	88	66 6	39	75 0	63	75 1	93	66 0	80	77 7	32	59 2
Total	195	100 0	195	100 0	63	100 0	63	100 0	132	100 0	132	100 0	92	100 0	141	100 0	103	100 0	54	100 0

TABLE NO 13

Neurological disturbances

		Sensory disturbances in right leg	Sensory disturbances in left leg	Impaired knee jerk right	Loss of knee jerk, right	Impaired knee jerk left	Loss of knee jerk left	Impaired ankle jerk right	Loss of ankle jerk right	Impaired ankle jerk left	Loss of ankle jerk left	Weakness of extensor hallucis right	Paralysis of extensor hallucis right	Weakness of extensor hallucis left	Paralysis of extensor hallucis left
Entire series	N = 212 P N = 212 C	5 3	11 3	4 1	0 2	1 2	0 2	6 0	1 3	4 2	1 3	3 0	0 2	2 0	0 2
Controls without past history of l b p	N = 71 C	0	0	0	0	1	0	0	0	0	0	0	0	0	0
Controls with previous l b p symptoms	N 141 C	3	3	1	2	1	2	0	3	2	3	0	2	0	2
Without clinical symptoms of l b p at the examination 1967	N = 99 P N – 153 C	3 3	2 2	1 1	0 1	0 2	0 1	3 0	1 2	0 1	1 2	1 0	0 2	1 0	1 2
Clinical symptoms of l b p found at the examination 1967	N = 113 P N 59 C	2 0	9 1	3 0	0 1	1 0	0 1	3 0	0 1	4 1	0 1	2 0	0 0	2 0	0 0

TABLE NO 14 I d x f R entgenol gi al Ch ng
R ents l gical f nd gs

	Entire seric				C s with out pa t h story of l b p		Corre spond g I s		C with pre io l b p symptom		Cr sponding I s		Clin sy npt n of l b p at the exa uiation 1967				W th ut cf ym pt ms of l b p t the exam tio 1967			
	I roband		Control		C ntrols		Probands		Controls v		Probands v		Proba ids		Contrcl		I rol ands		Controls	
0 N m iterj retal le	0		0		0	—	0	—	0	—	0	—	0	—	0	—	0	~	0	—
1 No chang s	6	3 1	19	9 7	9	14 3	2	3 2	10	7 6	4	3 0	4	4 3	14	9 9	2	1 9	5	9 3
2 Chai g s limited to thoracic spi ie	13	6 6	14	7 2	6	9 5	6	9 5	8	6 1	7	5 3	6	6 5	10	7 1	7	6 8	4	7 4
3 Changes li n ted to l ml ir spi e	27	13 8	37	19 0	11	17 5	5	7 9	26	19 7	22	16 7	13	14 1	24	17 0	14	13 6	13	24 1
4 Changes i i both thc racic and l mbar spine	149	76 5	125	64 1	37	58 7	50	79 4	88	66 6	99	75 0	69	75 1	93	66 0	80	77 7	32	59 2
Tc tal	195	100 0	195	100 0	63	100 0	63	100 0	132	100 0	132	100 0	92	100 0	141	100 0	103	100 0	54	100 0

TABLE NO 13

Neurological disturbances

		Sensory disturbances in right leg	Sensory disturbances in left leg	Impaired knee jerk right	Loss of knee jerk right	Impaired knee jerk left	Loss of knee jerk left	Impaired ankle jerk right	Loss of ankle jerk right	Impaired ankle jerk left	Loss of ankle jerk left	Weakness of extensor hallucis right	Paralysis of extensor hallucis right	Weakness of extensor hallucis left	Paralysis of extensor hallucis left
Entire series	N=212 P N=212 C	5 3	11 3	4 1	0 2	1 2	0 2	6 0	1 3	4 2	1 3	3 0	0 2	2 0	0 2
Controls without past history of l b p	N= 71 C	0	0	0	0	1	0	0	0	0	0	0	0	0	0
Controls with previous l b p symptoms	N=141 C	3	3	1	2	1	2	0	3	2	3	0	2	0	2
Without clinical symptoms of l b p at the examination 1967	N= 99 P N - 153 C	3 3	2 2	1 1	0 1	0 2	0 1	3 0	1 2	0 1	1 2	1 0	0 2	1 0	1 2
Clinical symptoms of l b p found at the examination 1967	N=113 P N- 59 C	2 0	9 1	3 0	0 1	1 0	0 1	3 0	0 1	4 1	0 1	2 0	0 0	2 0	0 0

TABLI NO 14 I idenc I Rontgc I g cal Chang R e i g n logical f d ig

	I nti	ne			C a w th o c pa t hi tory of l b p		Corre spond ng I s		C with pre i s l b p syn pto n		Corr sponding P s		Cl i sympt ms f l b p at the exam nati n 1967				Without l sym to n f l b p t the exa nination 1967			
	I robands		Controls		Cont ols		Prob nds		Controls		Probands		Prol ands		Controls		I rob nd		Controls	
0 Non i iterpr t ble	0		0	—	0		0	—	0	—	0	—	0	—	0	—	0	—	0	—
1 No changes	6	3 1	19	9 7	9	14 3	2	3 2	10	7 6	4	3 0	4	4 3	14	9 9	2	1 9	5	9 3
2 *Changes limited to* thoracic spine	13	6 (	14	7 2	6	*9 5*	6	*9 5*	*8*	*6 1*	7	5 3	6	6 5	10	7 1	7	6 8	4	7 4
3 Changes limited to lun bar pine	27	13 8	37	19 0	11	17 5	5	7 9	26	19 7	22	16 7	13	14 1	24	17 0	14	13 6	13	24 1
4 Chang in both thora c and lumbar spine	149	76 5	125	64 1	37	58 7	50	79 4	88	66 6	99	75 0	69	75 1	93	66 0	80	77 7	32	59 2
Total	195	100 0	195	100 0	63	100 0	63	100 0	132	100 0	132	100 0	92	100 0	141	100 0	103	100 0	54	100 0

TABLE NO 15 Localization of the Roentgenological Changes

Roentgenological findings

	Entire series				C s without past history of l b p		Corresponding P s		C s with previous l b p symptoms		Corresponding P s		Clin symptoms of l b p at the examination 1967				Without clin symptoms of l b p at the examination 1967			
	Probands	%	Controls	%	Controls	%	Probands	%	Controls	%	Probands	%	Probands	%	Controls	%	Probands	%	Controls	%
0 Non interpretable	0	—	0	—	0	—	0	—	0	—	0	—	0	—	0	—	0	—	0	—
1 No changes	6	3 1	19	9 7	9	14 3	2	3 2	10	7 6	4	3 0	4	4 3	14	9 9	2	2 0	5	9 3
2 Changes in the configuration	3	1 5	4	2 1	1	1 6	1	1 6	3	2 3	2	1 5	1	1 1	2	1 4	2	2 0	2	3 6
3 Changes in vertebrae	9	4 6	14	7 2	(	9 5	6	9 5	8	6 1	3	2 3	5	5 4	9	6 4	4	3 9	5	9 3
4 Changes in discs and ligaments	31	15 9	25	12 8	4	6 3	9	14 3	21	15 9	22	16 7	11	12 0	18	12 8	20	19 4	7	13 0
5 Changes in the configuration and vertebrae	12	6 2	14	7 2	7	11	5	9 5	7	5 3	7	5 3	7	7 6	14	9 9	5	4 9	0	—
6 Changes in the configuration and discs	38	19 5	36	18 5	8	12 7	15	23 8	28	21 2	23	17 4	19	20 7	26	18 4	19	18 4	10	18 5
7 Changes in vertebrae and discs	32	16 4	38	19 5	10	15 9	6	9 5	28	21 2	26	19 7	13	14 1	27	19 2	19	18 4	11	20 4
8 Changes in vertebrae discs and configuration	64	32 8	45	23 0	18	28 6	19	28 6	27	20 4	45	34 1	32	34 8	31	22 0	32	31 0	14	25 9
Total	195	100 0	195	100 0	63	100 0	63	100 0	132	100 0	132	100 0	92	100 0	141	100 0	103	100 0	54	100 0

TABLE NO 16 C f gura n Def n y u he Lumba S ne R e b olog l f d ng

	Lmt				C with o t p t h t ry of l b p		C r po d ng p		C w h pr u l b p y pt ms		Co l o d s P s		Cl y p l l p t th e or 1967				W h ym n of l b p t th x n n t on 1967			
	Pr b nds		C nt ols		Cont ol		Proband		Controls		Prob and		P ob nd		C ntrol		P oband		C t ols	
0 Non interpretabl	0		0		0	—	0	—	0	—	0	—	0	—	0	—	0	—	0	—
1 No changes	103	52 8	103	55 9	34	54 0	33	52 2	75	56 7	70	53 0	45	48 9	79	56 0	58	56 3	30	55 6
2 Incre sed lord sis	4	2 1	2	1 0	1	1 6	1	1 6	1	0 8	3	2 5	3	3 3	2	1 4	1	1 0	0	—
3 Stra ghtened lordo is	22	11 3	21	10 8	5	7 9	6	9 5	16	12 1	16	12 0	13	14 1	16	11 3	9	8 7	5	9 2
4 Sc l os s left-convex	25	12 8	23	11 8	10	15 9	9	14 3	13	9 8	16	12 0	14	15 2	17	12 1	11	10 7	6	11 1
5 Scoli sis r ght-c n e	31	15 8	29	14 8	6	9 5	11	17 6	23	17 5	20	15 2	12	13 0	17	12 1	19	18 4	12	22 2
6 Scoli is S-shaped	4	2 1	6	3 1	5	7 9	1	1 6	1	0 8	3	2 3	2	2 2	6	4 3	2	1 9	0	—
7 Scolio is and increased l rdosis	0	—	1	0 5	1	1 6	0	—	0	—	0	—	0	—	1	0 7	0	—	0	—
8 Scoli is and redu ed l rdo is	6	3 1	4	2 1	1	1 6	2	3 2	3	2 3	4	3 0	3	3 3	3	2 1	3	3 0	1	1 9
Total	195	100 0	195	100 0	63	100 0	63	100 0	132	100 0	132	100 0	92	100 0	141	100 0	103	100 0	54	100 0
Differ nt t n of s l s s																				
0 Non interpr table	1	0 5	1	0 5	1	1 6	1	1 6	0	—	0	—	0	—	0	—	1	1 0	0	—
1 N scoliosi	101	51 8	118	60 5	36	57 1	29	46 0	82	62 1	72	54 5	49	53 3	87	61 7	52	50 5	31	57 4
2 Pr bably not fi ed sl ght scol osis	39	20 0	31	15 9	11	17 5	12	19 0	20	15 2	27	20 5	20	21 7	25	17 7	19	18 4	6	11 1
3 Probal ly fi ed slight sc lio is	33	16 9	26	13 4	12	19 0	14	22 2	14	10 6	19	14 4	15	16 3	17	12 1	18	17 5	9	16 7
4 Probably not fi ed moderate scoli is	1	0 5	2	1 0	0	—	0	—	2	1 5	1	0 8	1	1 1	2	1 4	0	—	0	—
5 Probably fixed moderate s oliosis	19	9 8	15	7 7	3	4 8	6	9 6	12	9 1	13	9 8	7	7 6	10	7 1	12	11 6	6	11 1
6 Fixed pronounced scoliosis	1	0 5	2	1 0	0	—	1	1 6	2	1 5	0	—	0	—	0	—	1	1 0	2	3 7
7 Combinations	0	—	0	—	0	—	0	—	0	—	0	—	0	—	0	—	0	—	0	—
Total	195	100 0	195	100 0	63	100 0	63	100 0	132	100 0	132	100 0	92	100 0	141	100 0	103	100 0	54	100 0

TABLE NO 15 Localization of the Roentgenological Changes
Roentgenological findings

	Entire series				C s without past history of l b p		Corre sponding P s		C s with previous l b p symptoms		Corre sponding P s		Clin symptoms of l b p at the examination 1967				Without clin symptoms of l b p at the examination 1967			
	Probands	%	Controls	%	Controls	%	Probands	%	Controls	%	Probands	%	Probands	%	Controls	%	Probands	%	Controls	%
0 Non interpretable	0	—	0	—	0	—	0	—	0	—	0	—	0	—	0	—	0	—	0	—
1 No changes	6	3 1	19	9 7	9	14 3	2	3 2	10	7 6	4	3 0	4	4 3	14	9 9	2	2 0	5	9 3
2 Changes in the configuration	3	1 5	4	2 1	1	1 6	1	1 6	3	2 3	2	1 5	1	1 1	2	1 4	2	2 0	2	3 6
3 Changes in vertebrae	9	4 6	14	7 2	6	9 5	6	9 5	8	6 1	3	2 3	5	5 4	9	6 4	4	3 9	5	9 3
4 Changes in discs and ligaments	31	15 9	25	12 8	4	6 3	9	14 3	21	15 9	22	16 7	11	12 0	18	12 8	20	19 4	7	13 0
5 Changes in the configuration and vertebrae	12	6 2	14	7 2	7	11 1	5	9 5	7	5 3	7	5 3	7	7 6	14	9 9	5	4 9	0	—
6 Changes in the configuration and discs	38	19 5	36	18 5	8	12 7	15	23 8	28	21 2	23	17 4	19	20 7	26	18 4	19	18 4	10	18 5
7 Changes in vertebrae and discs	32	16 4	38	19 5	10	15 9	6	9 5	28	21 2	26	19 7	13	14 1	27	19 2	19	18 4	11	20 4
8 Changes in vertebrae discs and configuration	64	32 8	45	23 0	18	28 6	19	28 6	27	20 4	45	34 1	32	34 8	31	22 0	32	31 0	14	25 9
Total	195	100 0	195	100 0	63	100 0	63	100 0	132	100 0	132	100 0	92	100 0	141	100 0	103	100 0	54	100 0

TABLE NO 18 Transitional Vertebra
Roentgenological findings

	Frequencies				Cases with past history of lbp		Corresponding Ps		Cases with previous lbp symptom		Corresponding Ps		Clin symptoms of lbp at the examination 1967				Without clinical symptoms of lbp at the examination 1967			
	Probands		Controls		Controls		Probands		Controls		Probands		Probands		Controls		Probands		Controls	
0 Non interpretable	0	—	1	0 5	0	—	0		1	0 8	0	—	0	—	0	—	0	—	0	—
1 No transitional vertebra	166	85 ?	160	82 0	48	76 2	54	85 6	112	84 8	112	84 8	77	83 6	116	82 5	89	86 3	44	81 5
2 Symmetrical thoraco-lumbar transitional vertebra	8	4 2	4	2 1	0	—	2	3 2	4	3 0	6	4 5	3	3 3	2	1 4	5	4 9	2	3 6
3 Asymmetrical thoraco-lumbar transitional vertebra	3	1 5	3	1 5	2	3 2	0	—	1	0 8	3	2 3	1	1 1	3	2 1	2	2 0	1	1 9
4 Symmetrical lumbo-sacral transitional vertebra	3	1 5	6	3 1	5	7 ?	0	—	1	0 8	3	2 3	1	1 1	5	3 5	2	2 0	1	1 9
5 Asymmetrical lumbo-sacral transitional vertebra	7	3 6	8	4 2	2	3 2	2	3 2	6	4 5	5	3 7	4	4 3	5	3 5	3	2 8	3	5 6
6 Symmetrical thoraco-lumbar and asymmetrical lumbo sacral transitional vertebra	2	1 0	6	3 1	4	6 3	2	3 2	2	1 5	0	—	2	2 2	4	2 8	0	—	2	3 6
7 Asymmetrical thoraco-lumbar and asymmetrical lumbo sacral transitional vertebra	3	1 5	2	1 0	0	—	2	3 2	2	1 5	1	0 8	1	1 1	2	1 4	2	2 0	0	—
8 Asymmetrical thoracolumbar and symmetrical lumbo sacral transitional vertebra	1	0 5	2	1 0	0	—	0	—	2	1 5	1	0 8	1	1 1	2	1 4	0	—	0	—
9 Symmetrical thoraco lumbar and asymmetrical lumbo-sacral transitional vertebra	2	1 0	3	1 5	2	3 2	1	1 6	1	0 8	1	0 8	2	2 2	2	1 4	0	—	1	1 9
Total	195	100 0	195	100 0	63	100 0	63	100 0	132	100 0	132	100 0	92	100 0	141	100 0	103	100 0	54	100 0

TABLE NO 17 Spina Bifida
Roentgenological findings

	Entire series				C s with out past history of l b p		Corre sponding P s		C s with previous l b p symptoms		Corre sponding P s		Clin symptoms of l b p at the examination 1967				Without clin symptoms of l b p at the examination 1967			
	Probands	%	Controls	%	Controls		Probands	%	Controls	%	Probands	%	Probands	%	Controls	%	Probands	%	Controls	%
0 Non interpretable	0	—	1	0 5	0	—	0	—	1	0 8	0	—	0	—	0	—	0	—	1	1 9
1 No spina bifida	180	92 3	173	88 7	55	87 3	63	100 0	118	89 4	123	93 2	84	91 3	128	90 8	95	92 2	45	83 3
2 Spina bifida in the thoracic spine	0	—	0	—	0	—	0	—	0	—	0	—	0	—	0	—	1	1 0	0	—
3 Spina bifida in the lumbar spine and S1	15	7 7	21	10 8	8	12 7	0	—	13	9 8	9	6 8	8	8 7	13	9 2	7	6 8	8	14 8
4 Spina bifida in the thoracic spine and S1	0	—	0	—	0	—	0	—	0	—	0	—	0	—	0	—	0	—	0	—
Total	195	100 0	195	100 0	63	100 0	63	100 0	132	100 0	132	100 0	92	100 0	141	100 0	103	100 0	54	100 0

TABLE NO 18 T a t al V rt ra
R entg l gical f d gs

	I ur tre				C s u th ut pa t h to y of l b p		f rr sp nd ls P s		C with p e t s l b p ympt n		C t spo d ng l s		Cl symptoms of l b p at the ex an 1967				With ut cli sy pt ms f l b p at th e a ina n 1967			
	I ban l		C tr l		C tr l		I obanc ls		C nt ls		Pr b nd s		Pr ba ids		Contr ls		Prob nds		Contr ls	
0 N n interp t bl	0		1	0 5	0	—	0	—	1	0 8	0	—	0	—	0	—	0	—	0	—
1 N transitional vertebra	166	85 2	160	82 0	48	76	54	85 7	112	84 8	112	84 8	77	83 6	116	82 5	89	86 3	44	81 5
2 Symm etr al th rac lum bar tr nsiti nal vertebra	8	4 2	4	2,1	0		2	3 2	4	3 0	6	4 5	3	3 3	2	1 4	5	4 9	2	3 6
3 Asymmet i al th r o l mb r tr nsiti nal vert bra	3	1 5	3	1 5	2	3 2	0	—	1	0 8	3	2 3	1	1 1	3	2 1	2	2 0	1	1 9
4 Sy mm trical l mb sacral tra iti nal vertebra	3	1 5	6	3 1	5	7 9	0	—	1	0 8	3	2 3	1	1 1	5	3 5	2	2 0	1	1 9
5 Asym metrical lumbo s cral tran ti nal vertebra	7	3 6	8	4 2	2	3 2	2	3 2	6	4 5	5	3 7	4	4 3	5	3 5	3	2 8	3	5 6
6 Sym etrical th rac lu nb ar and symm etrical lumb sacral transiti nal vert bra	2	1 0	6	3 1	4	6 3	2	3 2	2	1 5	0	—	2	2 2	4	2 8	0	—	2	3 6
7 A ymmetrical th rac lumbar and asymm etrical lum b s ral transiti nal v rtebra	3	1 5	2	1 0	0	—	2	3 2	2	1 5	1	0 8	1	1 1	2	1 4	2	2 0	0	—
8 Asym metr al th rac lumb r a d sym metri al lu b sacral transitional vertebra	1	0 5	2	1 0	0	—	0	—	2	1 5	1	0 8	1	1 1	2	1 4	0	—	0	—
9 Symmetrical thoraco lumbar and asymmetrical lumbo-sacral transitional vertebra	2	1 0	3	1 5	2	3 2	1	1 6	1	0 8	1	0 8	2	2 2	2	1 4	0	—	1	1 9
Total	195	100 0	195	100 0	63	100 0	63	100 0	132	100 0	132	100 0	92	100 0	141	100 0	103	100 0	54	100 0

TABLE NO 19 Spondylolysis and Spondylolisthesis
Roentgenological findings

	Entire series				C s without past history of l b p		Corresponding P s		C s with previous l b p symptoms		Corresponding P s		Clin symptoms of l b p at the examination 1967				Without clin symptoms of l b p at the examination 1967			
	Probands		Controls		Controls		Proband %		Controls %		Probands %		Probands %		Controls %		Probands		Controls %	
0 Non interpretable	0	—	1	0 5	0	—	0	—	1	0 8	0	—	0	—	0	—	0	—	1	1 9
1 No spondylolysis or spondylolisthesis	186	95 4	183	93 8	63	100	58	92 1	120	90 9	128	97 0	89	96 7	134	95 0	97	94 2	49	90 7
2 Spondylolysis L3 L4 without spondylolisthesis	0	—	0	—	0	—	0	—	0	—	0	—	0	—	0	—	0	—	0	—
3 Spondylolysis L3 L4 with spondylolisthesis	0	—	1	0 5	0	—	0	—	1	0 8	0	—	0	—	1	0 7	0	—	0	—
4 Spondylolysis L4 – L5 without spondylolisthesis	0	—	1	0 5	0	—	0	—	1	0 8	0	—	0	—	1	0 7	0	—	0	—
5 Spondylolysis L4 L5 with spondylolisthesis	0	—	2	1 0	0	—	0	—	2	1 5	0	—	0	—	1	0 7	0	—	1	1 9
6 Spondylolysis L5 S1 without spondylolisthesis	1	0 5	2	1 0	0	—	0	—	2	1 5	1	0 8	0	—	1	0 7	1	1 0	1	1 9
7 Spondylolysis L5 – S1 with spondylolisthesis	8	4 1	5	2 7	0	—	5	7 9	5	3 7	3	2 2	3	3 3	3	2 2	5	4 8	2	3 6
8 Other localization	0	—	0	—	0	—	0	—	0	—	0	—	0	—	0	—	0	—	0	—
Total	195	100 0	195	100 0	63	100 0	63	100 0	132	100 0	132	100 0	92	100 0	141	100 0	103	100 0	54	100 0

TABLE NO. 20. Schmorl's Nodules
Roentgen Findings

	Ent r				C w th past history of l.b.p.		Corresponding Ps		C with previous l.b.p. symptom		Corresponding Ps		Cl symptoms of l.b.p. at the examination 1967				Without cl symptom of l.b.p. at the examination 1967			
	Proband		Control		Controls		Proband		Control		Probands		Probands		Control		Probands		Controls	
0 Non-interpretable	0		1	0 5	0		0		1	0 8	0	–	0	–	0	–	0	–	1	1 9
1 No changes	1 0	87 2	18[illegible]	93 4	57	90 5	53	84 1	125	94 7	117	88 6	80	87 0	132	93 7	90	87 4	50	92 4
2 Schmorl's nodules in the thoracic spine	9	4 6	6	3 1	4	6 3	2	3 2	2	1 5	7	5 3	6	6 5	5	3 5	3	2 8	1	1 9
3 Schmorl's nodules in the lumbar spine	6	3 1	3	1 5	0	–	3	4 8	3	2 2	3	2 2	1	1 1	2	1 4	5	4 9	1	1 9
4 Schmorl's nodules in both thoracic and lumbar spine	10	5 1	3	1 5	2	3.2	5	7 9	1	0 8	5	3 9	5	5 4	2	1 4	5	4 9	1	1 9
Total	195	100 0	195	100 0	63	100 0	63	100 0	132	100 0	132	100 0	92	100 0	141	100 0	103	100 0	54	100 0

TABLE NO 19 Spondylolysis and Spondylolisthesis
Roentgenological findings

	Entire series				C s with out past history of l b p		Corre sponding P s		C s with previous l b p symptoms		Corre sponding P s		Clin symptoms of l b p at the examination 1967				Without clin symptoms of l b p at the examination 1967			
	Probands		Controls		Controls		Probands %		Controls %		Probands %		Probands %		Controls %		Probands %		Controls %	
0 Non interpretable	0	—	1	0 5	0	—	0		1	0 8	0	—	0	—	0	—	0	—	1	1 9
1 No spondylolysis or spondylolisthesis	186	95 4	183	93 8	63	100	58	92 1	120	90 9	128	97 0	89	96 7	134	95 0	97	94 2	49	90 7
2 Spondylolysis L3 L4 without spondylolisthesis	0		0		0	—	0	—	0	—	0	—	0	—	0	—	0	—	0	—
3 Spondylolysis L3 L4 with spondylolisthesis	0		1	0 5	0		0	—	1	0 8	0	—	0	—	1	0 7	0	—	0	—
4 Spondylolysis L4 L5 without spondylolisthesis	0		1	0 5	0		0	—	1	0 8	0	—	0	—	1	0 7	0	—	0	—
5 Spondylolysis L4 L5 with spondylolisthesis	0		2	1 0	0	—	0	—	2	1 5	0	—	0	—	1	0 7	0	—	1	1 9
6 Spondylolysis L5 S1 without spondylolisthesis	1	0 5	2	1 0	0		0	—	2	1 5	1	0 8	0	—	1	0 7	1	1 0	1	1 9
7 Spondylolysis L5 S1 with spondylolisthesis	8	4 1	5	2 7	0	—	5	7 9	5	3 7	3	2 2	3	3 3	3	2 2	5	4 8	2	3 6
8 Other localization	0	—	0	—	0	—	0	—	0	—	0	—	0	—	0	—	0	—	0	—
Total	195	100 0	195	100 0	63	100 0	63	100 0	132	100 0	132	100 0	92	100 0	141	100 0	103	100 0	54	100 0

TABLE NO — Disc Degeneration
Roentgenological Findings

	Entire series				Controls with report history of lbp		Cases pending Ps		Cases with previous lbp symptoms		Cases spending ...		Clinical symptoms of lbp at the examination 1967				Without clinical symptoms of lbp at the examination 1967			
	Proband		Control		Controls		Probands		Controls		Proband		Probands		Controls		Probands		Control	
0 Non interpretable	0		1	0.5	0		0		1	0.7	0	—	0	—	0	—	0	—	1	[illegible]
1 No disc degeneration	105	53.8	133	68	51	81.1	40	63.5	82	62.1	65	49.2	52	56.5	100	[illegible]	53	51.5	33	61.1
2 Moderate disc degeneration in one level	47	24.1	21	10.8	6	9.5	14	22.2	15	11.4	33	25.0	28	30.4	14	[illegible]	19	18.4	7	13.0
3 Moderate disc degeneration in many levels	19	9.7	23	11.8	4	6.2	–	3.2	19	14.4	17	[illegible]	6	6.5	15	[illegible]	13	12.6	8	14.8
4 Advanced disc degeneration in one level	13	6.7	6	3.1	1	1.6	5	7.9	5	3.8	8	6.1	4	4.3	4	2.8	9	8.7	–	3.6
5 Advanced disc degeneration in many levels	7	3.6	10	5.1	1	1.6	1	1.6	9	6.9	[illegible]	4.5	0		7	5.1	7	6.8	3	5.6
6 Moderate and advanced disc degeneration in one or many levels	4	2.1	1	0.5	0	—	1	1.6	1	0.7	3	2.3	2	2.3	1	0.7	2	2.0	0	—
Total	195	100.0	195	100.0	63	100.0	63	100.0	[illegible]	100.0	132	100.0	92	100.0	141	100.0	103	100.0	54	100.0

TABLE NO 21 Osteoporosis
Roentgenological findings

	Entire series				C s with out past history of l b p		Corre sponding P s		C s with previous l b p symptoms		Corre sponding P s		Clin symptoms of l b p at the examination 1967				Without clin symptoms of l b p at the examination 1967			
	Probands		Controls %		Controls %		Probands %		Controls %		Probands %		Probands %		Controls %		Probands %		Controls %	
0 Non interpretable	0	—	0	—	0	—	0	—	0	—	0	—	0	—	0	—	0	—	0	—
1 No changes	181	92 8	178	90 6	54	85 7	58	92 1	124	93 9	123	93 2	83	90 2	128	91 3	98	95 1	50	92 6
2 Moderate osteoporosis	13	6 7	15	8 4	7	11 1	4	6 3	8	6 1	9	6 8	9	9 8	11	7 3	4	3 9	4	7 4
3 Pronounced osteoporosis	0	—	1	0 5	1	1 6	0	—	0	—	0	—	0	—	1	0 7	0	—	0	—
4 Pronounced osteoporosis with pathological fractures	1	0 5	1	0 5	1	1 6	1	1 6	0	—	0	—	0	—	1	0 7	1	1 0	0	—
Total	195	100 0	195	100 0	63	100 0	63	100 0	132	100 0	132	100 0	92	100 0	141	100 0	103	100 0	54	100 0

TABLE NO. [illegible] Disc Degeneration [illegible]
Roentgenological findings

	Entire series				Controls without history of l.b.p.		Corresponding probands		Controls with previous l.b.p. symptoms		Corresponding probands		Clinical symptoms of l.b.p. at the examination 1967				Without clinical symptoms of l.b.p. at the examination 1967			
	Probands		Controls		Controls		Probands		Controls		Probands		Probands		Controls		Probands		Controls	
0 Non interpretable	0		1	0.5	0		0		1	0.7	0	—	0	—	0	—	0	—	1	[illegible]
1 No disc degeneration	105	53.8	133	68.2	51	81.1	40	63.5	87	62.1	65	49.2	52	56.5	100	70.9	53	51.5	33	61.1
2 Moderate disc degeneration on one level	47	24.1	21	10.8	6	9.5	14	22.2	15	11.4	33	25.0	28	30.4	14	9.9	19	18.4	7	13.0
3 Moderate disc degeneration on many levels	19	9.7	23	11.8	4	6.2	2	3.2	19	14.4	17	12.9	6	6.5	15	10.6	13	12.6	8	14.8
4 Advanced disc degeneration on one level	13	6.7	6	3.1	1	1.6	5	7.9	5	3.8	8	6.1	4	4.3	4	2.8	9	8.7	2	3.6
5 Advanced disc degeneration on many levels	7	3.6	10	5.1	1	1.6	1	1.6	9	6.9	6	4.5	0	–	7	5.1	7	6.8	3	5.6
6 Moderate and advanced disc degeneration on many levels	4	2.1	1	0.5	0		1	1.6	1	0.7	3	2.3	2	2.3	1	0.7	2	2.0	0	—
Total	195	100.0	195	100.0	63	100.0	63	100.0	132	100.0	132	100.0	92	100.0	141	100.0	103	100.0	54	100.0

TABLE NO 23

Roentgenological evidence of disc degeneration in various age groups

Age	No disc degeneration						Moderate d d on one level						Moderate d d on many levels					
	Prob		Controls				Prob		Controls				Prob		Controls			
Years	M	F	M	F	I	II	M	F	M	F	I	II	M	F	M	F	I	II
20—29	10	7	10	7	7	10												
30—39	11	5	14	5	6	13	2		1				1					
40—49	19	11	23	17	10	30	5	6	4	2		6	4	2	1	4		5
50—59	13	13	24	18	18	24	16	6	3	1	3	1	6	1	11	2	1	12
60—69	12	4	8	6	9	5	6	5	6	4	3	7	3	2	5		3	2
70— <				1	1				1									
Total	65	40	79	54	51	82	29	18	14	7	6	15	14	5	17	6	4	19
Mean age	45 92±1 64	45 50±1 99	45 76±1 33	47 50±1 65	48 63±2 33	45 12±1 04	53 97±1 52	55 28±2 08	55 00±2 77	57 86±3 60			52 86±2 39	55 00±4 47	57 35±1 36	48 33±2 11		
Mean age	45 34 2 0		46 67 1 04		46 67 1 04		54 47 ±1 22		55 95 ±2 17				53 42 ±2 06		55 0 ±1 41			
T test	0 50 d f 236						0 60 d f =66						0 63 d f =40					

Age	Advanced d d on one level						Moderate and advanced d d						Advanced d d on many levels				
	Prob		Controls				Prob		Controls				Prob		Controls		
Years	M	F	M	F	I	II	M	F	M	F	I	II	M	F	M	F	I
20—29																	
30—39	1																
40—49	1	5	1	1		2											
50—59	2	3	1	1		2	3	1					1	2	2	4	
60—69	1		2		1	1			1			1	2	2	2	2	1
70— <																	
Total	5	8	4	2	1	5	3	1	1	—	—	1	3	4	4	6	1
Mean age	51 00±5 10	48 75±1 83	57 50±4 79	50 00±5 00			55 00±0	55 00±0	65 00±0				61 67±3 33	60 00±2 89	60 00±2 89	58 33±2 11	
Mean age	49 62 ±2 15		55 0 ±3 65				55 0 ±0		65 0 ±0				60 71 ±2 02		59 0 ±1 63		
T test	1 27 d f =17												0 66 d f =15				

Controls I — Without past history of low back pain — mean age with disc degeneration 55 61±1 26
Controls II — With previous l b p symptoms — mean age with disc degeneration 59 17±1 26

T ble no 23 co t

	P ob nd		C trol		Mod rat d se d g		Ad anced d se d s	
	Male	Female	Male	F mal	I obands	Cont ols	I obands	C ntrols
20 29 years		–	–	–	–	–	–	–
30 39 year	4 26 7	–	1 6 7	–	3 75 0	1 100 0	1 25 0	–
40 49 years	10 34 5	13 54 2	6 20 7	7 29 2	17 73 9	11 84 6	6 26 1	2 15 4
50 – 59 ye rs	28 68 3	13 50 0	17 41 5	8 30 8	29 70 7	17 68 0	12 29 3	8 32 0
60 – 69 years	12 50 0	9 69 2	16 66 7	6 46 2	17 77 3	15 68 2	4 18 2	7 31 8
0 –		1 100 0					1 100 0	
Total	54 45 4	36 47 4	40 33 6	21 27 6	66 73 3	44 72.3	24 26 7	17 27 7

TABLE NO 23

Roentgenological evidence of disc degeneration in various age groups

Age	No disc degeneration						Moderate d d on one level						Moderate d d on many levels					
	Prob		Controls				Prob		Control				Prob		Controls			
Years	M	F	M	F	I	II	M	I	M	F	I	II	M	I	M	F	I	II
20–29	10	7	10	7	7	10												
30–39	11	5	14	5	6	13	2		1				1					
40–49	19	11	23	17	10	30	5	6	4	2		6	4	2	1	4		5
50–59	13	13	24	18	18	24	16	6	3	1	3	1	6	1	11	2	1	12
60–69	12	4	8	6	9	5	6	5	6	4	3	7	3	2	5		3	2
70–<				1	1				1									
Total	65	40	79	54	51	82	29	18	14	7	6	15	14	5	17	6	4	19
Mean age	45 92 ± 1 64	45 50 ± 1 99	45 76 ± 1 33	47 50 ± 1 65	48 63 ± 2 33	45 12 ± 1 04	53 97 ± 1 52	55 28 ± 2 08	55 00 ± 2 77	57 86 ± 3 60			52 86 ± 2,39	55 00 ± 4 47	57 35 ± 1 36	48 33 ± 2 11		
Mean age	45 34 2 0		46 67 1 04		46 67 ± 1 04		54 47 ± 1 22		55 95 ± 2 17				53 42 ± 2 06		55 0 ± 1 41			
T test	0 50 d f 23(						0 60 d f (6						0 63 d f = 40					

Age	Advanced d d on one level						Moderate and advanced d d						Advanced d d on many levels				
	Prob		Controls				Prob		Controls				Prob		Controls		
Years	M	F	M	F	I	II	M	F	M	F	I	II	M	F	M	F	I
20–29																	
30–39	1																
40–49	1	5	1	1		2											
50–59	2	3	1	1		2	3	1					1	2	2	4	
60–69	1		2		1	1			1			1	2	2	2	2	1
70–<																	
Total	5	8	4	2	1	5	3	1	1	—	—	1	3	4	4	6	1
Mean age	51 00 ± 5 10	48 75 ± 1 83	57 50 ± 4 79	50 00 ± 5 00			55 00 ± 0	55 00 ± 0	65 00 ± 0				61 67 ± 3 33	60 00 ± 2 89	60 00 ± 2 89	58 33 ± 2 11	
Mean age	49 62 ± 2 15		55 0 ± 3 65				55 0 ± 0		65 0 ± 0				60 71 ± 2 02		59 0 ± 1 63		
T test	1 27 d f = 17												0 (6 d f – 15				

Controls I – Without past history of low back pain – mean age with disc degeneration 55 61 ± 1 26
Controls II – With previous l b p symptoms – mean age with disc degeneration 59 17 ± 1 26

TABLE NO. 4 Spondylosis
Roentgenological finding

	Entire series				Cases without past history of l.b.p.		Corresponding Ps		C with previous l.b.p. symptoms		Corresponding Ps		Cl symptoms of l.b.p. at the examination 1967				Without symptoms of l.b.p. at the examination 1967			
	Probands		Controls %		Controls		Probands		Controls		Probands		Probands %		Controls %		Probands		Controls	
0 Normal roentgenological	0		0		0		0	—	0		0	—	0	—	0	—	0	—	0	—
1 Slight spondylosis	31	15.9	53	27.2	24	38.1	13	20.6	23	22.0	18	13.7	18	19.6	41	29.1	13	12.6	12	22.2
2 Moderate spondylosis on one level	10	5.1	2	1.0	1	1.6	4	6.2	1	0.7	6	4.5	6	6.5	1	0.7	4	3.9	1	1.9
3 Moderate spondylosis on many levels	95	48.7	106	54.4	30	47.6	29	46.0	76	57.6	66	50.0	45	48.9	73	51.8	50	48.5	33	61.1
4 Advanced spondylosis on one level	2	1.0	1	0.5	0	—	0	—	1	0.7	2	1.5	1	1.1	1	0.7	1	1.0	0	—
5 Advanced spondylosis on many levels	14	7.2	10	5.1	3	4.8	6	9.5	7	5.3	8	6.1	8	8.7	7	5.0	6	5.8	3	5.6
6 Moderate and advanced spondylosis on one or many levels	43	22.1	23	11.8	5	7.9	11	17.7	18	13.7	32	24.2	14	15.2	18	12.7	29	24.2	5	9.2
Total	195	100.0	195	100.0	63	100.0	63	100.0	132	100.0	132	100.0	92	100.0	141	100.0	103	100.0	54	100.0

TABLE NO 4 Spondylosis
Roentgenological findings

	Entire series				Cases without past history of l b p		Corresponding probands		Cases with previous l b p symptom		Corresponding probands		Clin symptoms of l b p at the examination 1967				Without symptoms of l b p at the examination 1967			
	Probands		Controls		Controls		Probands		Controls		Probands		Proband		Control		Proband		Controls	
0 Non interpretable	0		0		0	–	0		0		0	–	0	–	0	–	0	–	0	–
1 No spondylosis	31	15.9	53	27.2	24	38.1	13	20.6	29	22.0	18	13.7	18	19.6	41	29.1	13	12.6	12	22.2
2 Moderate spondylosis on one level	10	5.1	2	1.0	1	1.6	4	6.2	1	0.7	6	4.5	6	6.5	1	0.7	4	3.9	1	1.9
3 Moderate spondylosis on many levels	95	48.7	106	54.4	30	47.6	29	46.0	70	57.6	66	50.0	45	48.9	73	51.8	50	48.5	33	61.1
4 Advanced spondylosis on one level	2	1.0	1	0.5	0	–	0		1	0.7	2	1.5	1	1.1	1	0.7	1	1.0	0	–
5 Advanced spondylosis on many levels	14	7.2	10	5.1	3	4.8	6	9.5	7	5.3	8	6.1	8	8.7	7	5.0	6	5.8	3	5.6
6 Moderate and advanced spondylosis on one or many levels	43	22.1	23	11.8	5	7.9	11	17.7	18	13.7	32	24.2	14	15.2	18	12.7	29	28.2	5	9.2
Total	195	100.0	195	100.0	63	100.0	63	100.0	132	100.0	132	100.0	92	100.0	141	100.0	103	100.0	54	100.0

TABLE NO 25

Roentgenological evidence of spondylosis in various age groups

Age	No spondylosis						Moderate spondyl on one level						Moderate spondyl on many levels						Advanced spondyl on one level						Moderate and advanced spondyl						Advanced spondyl on many levels				
	Prob		Controls				Prob		Controls				Prob		Controls				Prob		Controls				Prob		Controls				Prob		Controls		
Years	M	F	M	F	I	II	M	F	M	F	I	II	M	F	M	F	I	II	M	F	M	F	I	II	M	F	M	F	I	II	M	F	M	F	I
20–29	8	7	8	7	6	9	1						1		2		1	1																	
30–39	6		10	4	6	8	1						7	5	5	1		6							1										
40–49	5	2	7	8	8	7	3	1		2	1	1	16	15	21	14	1	34	1	1	1			1	4	5									
50–59	1	2	8		3	5	1	2					24	15	23	25	16	32							11	5	7	1	3	5	4	2	3		
60 69				1	1			1					7	4	7	7	1	3							11	6	12	3	2	13	6	2	5	2	3
70 <														1		1	1																		
Total	20	11	33	20	24	29	6	4	–	2	1	1	55	40	58	48	30	76	1	1	1	—	—	1	27	16	19	4	5	18	10	4	8	2	3
Mean age	34 50±2 11	34 09±3 92	39 55±1 95	37 00±2 47	39 58±1 88	37 76±1 22	41 (7±4 22	55 00±4 08	—	45 0 ±0			50 27±1 27	50 13±1 43	49 83±1 24	53 44±1 08			45 0 ±0	45 0 ±0	45 0 ±0	—			56 85±1 60	55 63±2 13	61 32±1 14	62 50±2 50			61 00±1 63	60 0 ±2 89	61 25±1 83	65 0 ±0	
Mean age	34 35 ±1 91		38 58 ±1 53				47 00 ±3 59		45 0 ±0				50 21 ±0 94		51 46 ±0 85				45 0 ±0		45 0 ±0				56 36 ±1 24		58 96 ±2 54				60 71 ±1 37		62 0 ±1 53		
T test	1 73 d f −82						0 56 d f =10						0 99 d f =199						—						0 92 d f =64						0 63 d f =22				

Control I – Without past history of low back pain – mean age with spondylosis 51 99±0 87 years
Controls II With previous low back pain symptoms – mean age with spondylosis 56 03±1 60 years

T 11 n 25 t

	Pr band		Co trols		Mod rat spo d		Ad c d p n l	
	Mal	F nal	Mal	I al	I r ba ds	Cc tr ls	I ob d	Controls
20 29 years	2 28 6	—	2 9 6	—	100 0	2 1000	—	—
30 39 yea	9 60 0	5 100 0	5 33 3	1 20 0	13 92 9	6 100 0	1 7 1	—
40 49 year	24 8 8	22 91 7	22 75 9	16 66 7	35 76 1	37 97 4	11 23 9	1 2 6
50 59 years	40 97 6	24 92 3	33 80 5	26 100 0	42 65 6	48 81 4	22 34 4	11 18 6
60 69 years	24 100 0	13 100 0	24 100 0	12 92 3	23 62 2	14 37 8	14 37 8	22 62.2
0		1 100 0	—	1 100 0	—	1 100 0	1 100 0	—
Total	99 83 2	65 85 5	86 72 3	56 73 7	115 70 1	108 76 1	49 29 9	34 23 9

TABLE NO 25

Roentgenological evidence of spondylosis in various age groups

Age	No spondylosis						Moderate spondyl on one level					
	Prob		Controls				Prob		Controls			
Years	M	F	M	F	I	II	M	F	M	F	I	II
20–29	8	7	8	7	6	9	1					
30–39	6		10	4	6	8	1					
40–49	5	2	7	8	8	7	3	1		2	1	1
50 59	1	2	8		3	5	1	2				
60–69				1	1			1				
70– <												
Total	20	11	33	20	24	29	6	4	–	2	1	1
Mean age	34 50±4 11	34 09±3 92	39 55±1 95	37 00±2 47	39 58±1 88	37 76±1 22	41 67±4 22	55 00±4 08	–	45 0 ±0		
Mean age	34 35 1 91		39 58 +1 63				47 00 ±3 59		45 0 ±0			
T test	1 73 d f 82						0 56 d f = 10					

Age	Moderate spondyl on many levels						Advanced spondyl on one level					
	Prob		Controls				Prob		Controls			
Years	M	F	M	F	I	II	M	F	M	F	I	II
20–29	1		2		1	1						
30–39	7	5	5	1		6						
40–49	16	15	21	14	1	34	1	1	1			1
50 59	24	15	23	25	16	32						
60–69	7	4	7	7	1	3						
70– <		1		1	1							
Total	55	40	58	48	30	76	1	1	1	–	–	1
Mean age	50 27±1 27	50 13±1 43	49 83±1 24	53 44±1 08			45 0 ±0	45 0 ±0	45 0 ±0			
Mean age	50 21 ±0 94		51 46 ±0 85				45 0 ±0		45 0 ±0			
T test	0 99 d f =199						–					

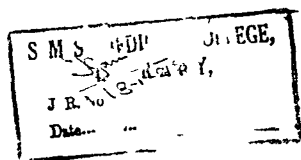
Age	Moderate and advanced spondyl						Advanced spondyl on many levels				
	Prob		Controls				Prob		Controls		
Years	M	F	M	F	I	II	M	F	M	F	I
20–29											
30–39	1										
40–49	4	5									
50 59	11	5	7	1	3	5	4	2	3		
60–69	11	6	12	3	2	13	6	2	5	2	3
70– <											
Total	27	16	19	4	5	18	10	4	8	2	3
Mean age	56 85±1 60	55 63±2 13	61 32±1 14	62 50±2 50			61 00±1 63	60 0 ±2 89	61 25±1 83	65 0 ±0	
Mean age	56 36 ±1 24		58 9(±2 54				60 71 ±1 37		62 0 ±1 53		
T test	0 92 d f =64						0 63 d f =22				

Controls I – Without past history of low back pain – mean age with spondylosis 51 99±0 87 years

Controls II – With previous low back pain symptoms – mean age with spondylosis 56 03±1 60 years

BJÖRN MAURITZ PERSSON

GROWTH IN LENGTH OF BONES IN CHANGE OF OXYGEN AND CARBON DIOXIDE TENSIONS



ACTA ORTHOPAEDICA SCANDINAVICA
SUPPLEMENTUM NO 117
MUNKSGAARD COPENHAGEN 1968

ERRATA Acta orthop scandinav suppl 117

Page 5 line 2 omit Review of literature on leg length inequality
Page 8 line 1 from below Mugrove read Musgrove
Page 37 line 2 t=3 42xx , read t=3 18xx
line 5 t=0 23- , read t=0 34-
Page 38 group 2, animal 4 EDV III , read EDV II
Page 39 group 1, animal 5 DZH IV 540 530 510 , read DZH VI 480 490 460
group 1, Mean growth 501 496 482 read 498 494 480
group 1, Mean diff —5 —13 read —4 —14
group 1, Stand dev 14 70 14 26 , read 15 02 14 65
group 1, t value —1 63 —4 28 read —1 31 —4 32
significances are not changed
group 2 last animal EMV IV read EMV VI
Page 46 group 1 last animal AKV V read AKV I
Page 49 group 1 animal 7 from below CVS III , read CSV III
Page 55 group 1, animal 3 DLV II , read DLV III
group 1 Add
DAH II 480 430 380
DAH IV 500 460 420
DAV I 510 500 470
DAV II 520 510 500
group 1 n value 12 12 read 16 16
Page 56 group 1 in Table 19 Add
DAH I 540 540 510
DAH III 530 530 510
DAV IV 530 530 510
group 1 n value 11 11 , read 14 14
Page 57 line 17 t=1 21- read U=1 76-
t=0 09- , read t=0 01-
Page 59 group 1 animal 5 DPH IV in period +1 430 , read 330
group 1 animal 14 FBH IV 420 read FBH IV 410
group 3 animal 14 omit duplicated EAV III
Page 60 group 2 in Table 21 animal 7 DXV II 460 540 510 read
DXV I 580 590 570
group 2 Mean growth 482 500 497 read 496 506 503
group 2 Mean diff +18 —3 read +10 —2
group 2 Stand dev 27 28 36 74 read 14 14 35 98
group 2 t value +1 96 —0 27 read +2 12 —0 91
significances are not changed
Page 65 group 2 animal 10 GGH I read GHH I
Page 67 line 2 from below between the seven read between the five
Page 69 group 1 animal 1 BHM I read BMH I
group 3 animal 9 DDV I 460 460 read DDV I 460 440
Page 71 group 1 in Table 27 animal 6 BTH V read BTV V
Page 74 in Table 29 animal 16 EPH I read HPH I
Page 91 line 13 ultraviolet microscopy read ultraviolet fluorescence microscopy

GROWTH IN LENGTH OF BONES
IN CHANGE OF OXYGEN
AND CARBON DIOXIDE TENSIONS

To the memory
of my father

ACTA ORTHOPAEDICA SCANDINAVICA
SUPPLEMENTUM No 117

From the Department of Orthopedic Surgery University Hospital Lund Sweden
(Head Professor Gunnar Wiberg) and the Institute of Physiology
Laboratory of Aviation and Naval Medicine University of Lund, Sweden

GROWTH IN LENGTH OF BONES IN CHANGE OF OXYGEN AND CARBON DIOXIDE TENSIONS

BY

BJÖRN MAURITZ PERSSON

MUNKSGAARD COPENHAGEN 1968

Statistical adviser Leif Pedersen, B A

LUND 1968
RAHMS BOKTRYCKERI AB LUND

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INTRODUCTION

This work is part of a research into the longitudinal growth of bones against the clinical background of leg length disparity in children. Hundreds of publications have appeared during the last century describing different conditions resulting in stimulated or retarded growth in length. The clinical aspect of this problem was reviewed by Goff in 1960 citing 638 references on the topic. The acceleration of growth in length reported during the last century after fractures osteomyelitis or arterio-venous fistulae in limbs has led to series of experimental efforts to induce increased growth rate for therapeutic equalizing of leg length disparity caused by one sided stimulation as mentioned or by retardation after poliomyelitis epiphyseal growth plate injuries or congenital defects. These experiments were recently reviewed and analysed by Sunden (1967) in a table listing about 120 papers. Periosteal stripping curettage of the medullary cavity implantation of a great number of different materials into the medullary cavity plugging of the cavity fracturing of bones application of heat, electricity roentgen radiation ultrasound shortwave diathermy venous stasis, creation of femoral arterio-venous fistulae immobilisation nerve sectioning nerve root sectioning sympathectomy and mechanical stress and strain have all been tried. Summarizing these observations there is no doubt that direct trauma to the growing long bones whether caused by fracture periosteal stripping or medullary plugging (Hansson 1967) does cause a certain longitudinal growth acceleration in a considerable percentage of cases except when the epiphyseal growth plate itself is injured or the trauma is minimal. The same applies to chronic inflammation, whether caused by infection rheumatoid arthritis (Brattstrom 1963) implantation of foreign materials or other necrotizing influences. Finally indirect measures such as arterio-venous fistulae and peripherial nerve divisions have shown an enchancement of growth in length (Sunden 1967) while induced venous stasis has produced more diverging results.

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Mechanism of overgrowth

Arterial hyperaemia

The underlying cause of longitudinal over growth is mostly considered to be increased arterial blood flow *in the growth plate* regions (*Langenskiold* 1957, *Hansson & Wiberg* 1963 *Vanderhoeft* et al 1963) This should apply during fracture healing (*Levander* 1929) and after *periosteal* loosening of a diaphysis (*Ollier* 1867, *Brodin* 1955 *Elo* 1960) as well as after experimental interruption of the intramedullary vessels (*Ferguson* 1933) By blocking the medullary canal (*Cavadias & Trueta* 1965) this interuption is made more lasting and will cause a compensatory increase in blood flow to the metaphysis through vessels near the growth plate thereby inducing an increased growth rate Also when the femoral arterio venous fistula was introduced as a measure for growth stimu lation the effect was believed to be mediated through a hyperaemia distal to the fistula (*Janes & Musgrove* 1950) Later studies on the actual blood flow in these cases have however shown a decreased blood flow distally (*Holman* 1955) Registration of growth in length and of the blood flow in bone under the same circumstances was made by *Sunden* (1967) He demonstrated an increased growth after peripherial nerve division measured by oxytetracycline labelling, and a simultaneous increase in bone blood flow measured as heat clearence This is in support of the hyperaemia theory further strengthened by the fact that the same growth acceleration was achieved by immobilisation through Achilles tendon division in rabbits as well Immobilisation in plaster of rabbit legs has been shown to cause an increase in pO, and pH of the intramedullary blood as well as an increased Sr^{8} clearence (*Semb* 1966) which also favours the hyperaemia theory The important role played by the skeletal blood flow has also led to succesive attempts to stimulate growth in length by direct implantation of a patent artery into a long bone (*Dickerson* 1966)

Venous stasis

The major opposition to the theory of arterial hyperaemia has come from authors believing a venous stasis to be the causative agent in cases of one sided over growth in length This should be the mechanism with trauma to a long bone as well as in femoral arterio venous fistulae and in venous stasis induced by tourniquet (*Hutchison & Burdeaux* 1954) Arterio venous fistula is the most reliant stimulant of growth experimentally and clinically generally leading to a more reliable increase in length than trauma and inflammation (*Broca* 1856 *Janes & Mugrove* 1950 *Cooley* et al 1960, *Hiertonn* 1961 *Janes &*

Jennings 1961) *Birnstingl* (1962) reported 2 3 cm increase in the femur and 4 3 cm increase in the tibia in a case of a femoral fistula demonstrated by serial femoral angiography He considered this dominating tibial growth acceleration to be supportive evidence for the hypothesis that venous stasis caused by the fistula, was the causative mechanism. This opinion seems to be shared by *Colt & Iger* (1963) and by *Keck & Kelly* (1964) who angiographically demonstrated an arterial back flow in the distal vein they called this an active venous stasis The haemodynamics of arterio-venous fistulae have been subjected to several investigations (*Holman* 1955 *Henrie* et al 1959 *Hillman* et al 1959 *Stein* et al 1959 *Ingebrigtsen* et al 1963 *Weinman* et al 1964) Venous stasis distally is a common finding although the collateral circulation which is very pronounced and the back flow in the veins both complicate the interpretation regarding effects on the growth plates *Hillman* et al (1959) conclude about induced stasis and arterio-venous fistulae "venous stasis is the common denominator in these two conditions which produce limb overgrowth and would seem to be related etiologically The exact mechanism by which venous stasis produces limb over growth is still unexplained Venous stasis induced for therapeutic purposes was first reported by *Helferich* (1887) who claimed to have reduced leg inequality in two children by prolonged tourniquet stasis of the shorter legs The method was repeated later in humans (*Bier* 1903) and in animal experiments (*Borel* 1922 *Kishikawa* 1936 *Peck* 1957 *Colt & Iger* 1963 *Keck & Kelly* 1964) with diverging results In 1948 Servelle published a series of venographically verified unilateral congenital venous abnormalities with stasis in 14 humans whose affected legs were 0 8—9 6 cm longer than the contralateral ones while no differences could be found in any of 25 patients with chronic lymphoedema elephantiasis *Hutchison & Burdeaux* (1954) are among those who found induction of venous stasis to stimulate the growth rate They express the opinion that venous stasis is responsible for the over growth not only in arterio-venous fistulae but also in fractures and osteomyelites Attempts to measure the actual blood flow in bone during venous stasis have been contradictory (*Shaw* 1964 *Walderrama & Trueta* 1965 *White & Stein* 1965)

Growth stimulating substances

No successfull efforts seem to have been made to demonstrate the mechanism by which a venous stasis is supposed to accelerate the growth *Foster & Kirtley* (1959) believe that possibly the stasis supplies an increase of growth stimulating substances This has also been proposed as a mechanism in other conditions with over growth of bones (*Lacroix* 1947 *Wray & Goodman* 1961) Even when dealing with leg length inequality as here one must not forget the possibility of

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affecting living cells Physical variation of either or both of these might influence the rate of growth of bone They observed an increased growth in length in both dogs and rats using an electrically heated sling around the *femora*, but unfortunately the method produced such a necrotizing effect that even fractures resulted Heating was attempted also by *Ring & Lee* (1958) using carbon resistors implanted into the bony epiphysis of the ulna in rabbits but they induced only increase in width.

The importance of the temperature factor has thus been observed but no conclusive results have been presented as to the possibilities of using it for growth rate alterations

The oxygen factor

Concerning the possibilities of inducing changes in the growth of long bones by alteration of the oxygen tension no reports can be found in the literature In spite of this many authors mention increase in oxygen availability as a probable factor in observed accelerations in bone growth Since the discovery of oxygen by *Priestley* in 1774 much has been written regarding oxygen in medicine This literature has been reviewed by *Bean* (1945 1964) and with regard to the use of oxygen at increased barometric pressure also by *Linehan* (1964) and by *Jacobson* et al (1965) The fundamental importance of oxygen in general has even led to trials of injection of gaseous oxygen in arteries in conditions of ischaemia (*Fey & Boxberg* 1956) as well as injection of diluted hydrogen peroxide but not in connection with growth studies

Tissue culturing technics have been employed to study oxygen effects on growth in general *Cooper* et al (1958) studied the growth of animal cells and virus *Ollodart & Blair* (1965) demonstrated increased growth of bacterias in oxygen tensions up to 1 atm abs (athmosphere absolute=760 mm Hg) and bacteriostasis on further increase of the oxygen tension *Nelson* (1958) studied the early development of chick and frog embryos and recorded some stimulation in certain stages *Goldhaber* (1958) observed increased osteoclastic activity of cultured bone at 95 per cent oxygen in the gaseous phase at 1 atm abs and pointed out the similarity to the effects caused by parathyreoid hormone *Vaes & Nicols* (1962) found increased metabolism in rat bone cultures at increased oxygen tension *Shaw & Basset* (1967) cultured chick embryo tibiae under different oxygen concentrations in the gaseous phase and found maximal osteogenesis at 35 per cent but at 5 per cent and at 95 per cent of oxygen there was a pronounced decrease in osteogenesis and chondrogenesis

The effects of increased oxygen tension on healing of standardized surgical wounds have been studied by *Lundgren & Sandberg* (1965) reporting decreased healing in normal rats and acceleration in anemic rats during *hyperbaric*

local liberation of stimulating substances of the *same type* as in cases of total body growth abberations, that is hormonal and nutritional factors, but acting locally

Pressure and tension

For completeness it is necessary to mention also mechanical loading and un loading as measures to influence growth of bones although this has very little application in this investigation The temporary epiphyseodesis with staples according to Blount (*Blount & Clarke* 1949) is proof of the growth retarding possibilities using pressure, demonstrated previously by *Wegner* (1878) also using staples and wire cerclage The pressure necessary to stop growth has been determined (*Strobino* et al 1952, *Blount & Zeiter* 1952) The possibility that growth can be accelerated by tension has not been demonstrated convincingly (*Smith & Cunningham* 1957)

Increase in temperature

The living cell and its enzymatic, oxidative systems, must have some optimal temperature and oxygen tension for the physiological processes to proceed normally As over growth can be induced there might be a zone left on the side of the normal temperature or oxygen tension where an increased turn over could take place The temperature factor has been paid attention to in the literature Supposing increase in temperature to be a common denominator for all conditions of over growth mentioned above *Granberry & Janes* (1963) tried to heat a growth plate in dogs by microwave diathermy but with no positive result On the other hand *Doyle & Smart* (1963) observed increased growth in rats after short wave diathermy and so did *Asnoub* (1958) by housing mice for 4 weeks at two extreme temperatures recording an increase in tail length of 15 per cent in the warmer environment

After creating arterio venous fistulae *Janes & Musgrove* (1950) observed increased longitudinal bone growth in dogs and they recorded an increased medullary temperature in the femur of the operated legs compared to the un operated *Brodin* (1955) measured the intramedullary temperature in the tibia after one sided periosteal loosening but observed a temperature variation within the cavity of such a magnitude that side comparisons were impossible *Richards & Stofer* (1959) also tried to study the temperature factor They say temperature and oxygen tension are probably the two most important physical variables

and carbon dioxide changes which have to be considered during change in the environmental oxygen tension Regarding the controversial opinions about *hyperaemia or venous stasis as the responsible factor for accelerated growth in* length it has been considered to be of great interest to see whether a direct alteration in the respiratory oxygen tension can induce a change in the growth rate especially as the oxygen factor itself on the cellular plane must be of a key importance, not earlier studied in this respect Except for the oedema promoting tendency a major character of venous stasis compared to arterial hyperaemia is probably the lower tissue tension of oxygen and higher tension of carbon dioxide and consequently a study of the influence of these gases on growth could shed some light on the problem of overgrowth of bones increasing our know ledge about oxygen therapy in general and about the physiology of the growing epiphyseal plate in particular

oxygen therapy at intervals, but in dogs augmented healing has been reporte (Beckham & Hitchcock 1965) Studying the survival of split skin grafts in 48 humans Perrins (1967) recorded an increase in the taken area of 29 per cent and an increase in complete graft taking from 17 to 64 per cent after hyperbaric oxygenation at 2 atm abs of pure oxygen breathing for two hours twice daily during three days after operation

Also in the case of fracture healing oxygen has lately aroused interest. Coulson et al (1966) report accelerated healing in femoral fractures of the rat at hyperbaric oxygenation in intervals for 1—3 weeks, tested by mechanical resistance and radioactive calcium activity This finding is complemented by Makley et al (1967) observing impaired healing of fractures in rats at reduced barometric pressure corresponding to 18 000 feet of altitude Periosteal proliferation in mice has been studied by Manspeizer & Tonna (1967) who found decreased proliferation at 5 per cent oxygen and increased at 100 per cent oxygen in the environment measured by tritiated thymidine and autoradiography A search of the literature has actually revealed one work mentioning also growth in length and the influence of increased oxygen tension and that is Wright & Howard Flanders (1957) investigating the growth in length of mice tails after roentgen radiation combined with 100 per cent of oxygen in an environment of atmospheric pressure varying from 0 1 to 3 0 atm abs They found radiosensitivity decreased during hypoxia and increased during hyperoxia as measured by the length of the tails In a control group they varied the oxygen tension without radiation and did not observe any effects on the length of the tails The data given and the short period of treatment do not allow any conclusions to be drawn concerning the unplanned observations on the relationship between longitudinal growth of bones and the environmental partial pressure of oxygen

Purpose of investigation

The purpose of this investigation can now be advanced in the light of what is said above, concerning factors influencing longitudinal bone growth especially the oxygen factor In the literature on over growth of bones increase in the oxygen tension is almost regularly mentioned as a hypothetic cause of the growth stimulation but no experimental efforts to prove this have appeared Preliminary observations on change in the longitudinal growth of the proximal tibial metaphysis of rabbits during hyperbaric oxygenation for repeated short intervals during a single day have been published earlier (Persson 1967) and the aim has been to extend the study for more exact documentation of the effects and for evaluation of such secondary consequenses, as oxygen toxicity

couple of days before the experiments The hutches were in door with daylight, with electric light added during winter between about 07 00 and 17 00 The temperature in the hutches was about 18—23°C Humidity was not specially controlled The rabbits were fed on pellets and water ad libitum and by milk from their mothers as long as they suckled them During the 8 hrs of treatment (see later) both test and control rabbits were taken away from the mothers but were given pellets and water in the treatment boxes They were weighed on the first and on the last day of the experiment

After the choice of rabbits to be used for the study one had to consider which aberrant animals to exclude during the experiments.

Exclusion of animals

Among young rabbits at the time of weaning a considerable percentage will die or be temporarily diseased Further more some of them will be regaining health during the time of growth measurements and this will give an increased deviation in the figures of growth making necessary very long series unless these factors could be reduced in a way not influencing the reliability of the effects to be studied This problem is of special importance when growth rate investigations are performed for studying influences on the whole rabbit, comparing different individuals in comparison to right and left side studies in the same animal This is consequently an added difficulty but the method used in this way allows for increased possibilities The preliminary studies (*Persson* 1967) had shown that some principles had to be introduced for exclusion of unhealthy animals because even grossly undetectable diseases in the rabbits could severely affect the growth rates recorded It was thought unsatisfactory in this investigation to exclude animals below a certain weight (*Hansson* 1967) as different breeders could have different standard weights a a certain age because of genetic or nutritional factors It was also thought insufficient to exclude animals because of clinical impression of disease (*Hansson* 1967 *Sunden* 1967) and after the preliminary experiences the following conditions for excluding animals were adopted

1 Spontaneous death during the experiment (only complete observation series were used)
2 Loss of weight between the start and the end of the experiment (precision of the instrument ± 5 grams)
3 Diarroea observed during the experiment
4 Unacceptable quality of preparations for microscopy (allowing for less than 5 readings)

CHAPTER 2

MATERIAL AND METHODS

Choice of animal

Because of the toxicity of pure oxygen inhaled for an extended period it was evident that the method chosen, should allow determination of growth rates with a high accuracy over very short periods of time that is about one day Therefore the intravital tetracycline labelling method seemed to be the best for quantitative measurements (see later) Concerning the choice of animal it was clear that it had to be some relatively fast growing type to allow observations on changes during the short times made possible by the oxygen toxicity and secondly, it had to be easily available for the comparatively long series necessary, in a study dealing with comparisons between different animals and not as hitherto for the above mentioned method between the right and left sides These conditions allow for the use of rabbits rats mice and guinea pigs but as the method hitherto had been used for longitudinal growth estimations mainly in rabbits, (*Hulth & Olerud* 1962 *Hansson* 1964 and 1967 *Sunden* 1967) this favoured the choice of rabbits, especially as they had often been used in bone growth investigations in general as well as in the literature on oxygen toxicity and breathing physiology (*Dittmer & Grebe* 1958) The rabbits used were always white to make the intravenous injections easier in the young animals used aged between 27 and 42 days at the day of treatment The age was chosen because of the easier preparation and the greater growth rate during this time (*Hansson* 1967) The sex of the animal was not taken into account (*Hansson* 1967)

Care of animals

The general care of animals was the same in test and control as follows Rabbits were bought from three breeders who had noted the day of birth and were transported to the hutches with their mothers They lived together for a

Table 1

Specification of animals excluded d ring the invest gation The groups are in accordance with the l st of principles for exclusions g ven in text

1 Spontaneous death		2 Loss of weight		3 Diarroea		4 Unacceptable preparations		5 Abnormal growth		6 Single animal	
Test	Contr	Test	Contr	Test	Contr	Test	Contr	T st	Contr	Test	Contr
QH III	FGH III	EVV III	FRH III	CIH II	CIV II	FRH II	VV IV	EEV III	OV I	NH V	CZH III
QH IV	CAV III	GXV I	FRV III	CIV I	CLH III	EUH I	GUH I	FGH I	NH IV	DBH III	BVV I
VH I	DDH II	EMV V	DYV III	DOV I	CTV I	GTV III	EEV I	GCV V	EKH I	BRV I	
VH III		CSH I	EEV II	DRH IV	DOV III	GUH IV	CKH IV	DEH III	DOH IV		
CSV I		EBV I	CIH IV	FDH V	DPV II	EEH III	CKV I	DFH I	DBH I		
CSV II		CZV III	CIV IV	CZH IV	DRH I	CQH III	ENV IV	HFH II	DBV II		
CTH III		DKV V	EAV I	CZH II	DRH III	CRV II	EPH II	EDV IV	DIV V		
CTV III		DIV II	ECV I	CZV I	CZV II	CKH I	FZH I	LEV IV	GCH V		
DPH I		GDH II	CZH I	DBH II	DKV IV	CKV II	ERH IV	EMV III	FZV I		
DBV I		BRV II	CZV IV	GAH II	GEH II	DIH III	BRH IV	FVH I	HQH V		
DKV III		CXH IV	DKV I	BRH II	FVV IV	GEH I		FZV III	HQV IV		
GDV II		DGV III	ENV III	BVH II	FUH VI	ENH III			BTV III		
ECH II		BVV II	FVH V		BVH I	ENV V					
		CAV I	FVV III		DEV I	GDV III					
			ESV I			FVV V					
			BRH III			FVH IV					
			DGH I			FXH I					
			DGH III			FXH II					
			DCV I			ERH I					
						ESV III					
						BRV III					
						DDH III					
13	3	14	19	12	14	22	10	11	12	3	2

5 Disease made evident by abnormal growth rate, defined as being more than 100 microns below the arithmetic mean of litter mates exposed to the same treatment (observed during any of the three 24 hrs periods measured)

6 Animal left single in a litter after exclusions above

(*For definitions of preparations readings and growth periods* see later in this chapter)

These six principles have been followed throughout the investigation with the following comments Regarding point 1 there are no exceptions complete readings were made impossible by the death of the animal Point 2 has proved to be well founded on the fact that decreased growth rate was practically always observed in animals with decrease in weight and after some time these animals where not prepared for microscopy at all Point 3 was used in the way that animals being soiled by their diarroea were excluded Regarding point 4 30 animals were accepted in the beginning of the investigation with less than five readings, but only in cases where no difference between consecutive time periods were recorded With regard to point 5 finally, 2 animals were accepted also in the beginning and in cases where the difference between consecutive periods was not mor than 10 microns, thereby negligibly affecting the calculations A full account of excluded animals is given in Table 1 Each animal is given with its identification number the last letter plus the following roman figures designating the number within its litter and the first one or two letters designating the litter This allows one in reading the tables, given in the results to identify the origin of the excluded animals The total number of excluded animals is 148 but this should be compared to the total number of animals before this exclusion that is 1079 giving a reasonable percentage of exclusion for rabbits at this age In all 13 animals died spontaneously after registration at the institution but before any treatment and are therefore not listed in Table 1 The distribution of animals given in Table 1 further shows that spontaneous deaths were more common among test animals, of which 4 died during administration of the maximal doses of oxygen and 4 while given the minimum doses This is further discussed later In the group of unacceptable preparations there are also more test animals but the distribution is even over the whole material comprising 532 tests and 399 controls In the other groups there is no remarkable difference between the number of test and control animals excluded.

From the studies of *Hansson* (1967) it was known that there was a succesive decrease in growth rate after the age of 30 days (Fig. 15) but no correlation between weight and growth within each litter It was therefore considered to be of interest to see how the *selection principles* used in this study influenced on a possible correlation between these factors There was a considerable number of control animals with notes on age weight and growth in length of the proximal tibial metaphysis measured on the same day as they were weighed In all 237 animals were grouped according to age and analysed regarding a correlation between growth and weight at the given age It turned out to be a

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QH IV	CAV III	GXV I	FRV III	CIV I	CLH III	EUH I	GUH I	FGH I	NH IV	DBH III	BVV I
VH I	DDH II	EMV V	DYV III	DOV I	CTV I	GTV III	EEV I	GCV V	LKH I	BRV I	
VH III		CSH I	EEV II	DRH IV	DOV III	GUH IV	CKH IV	DEH III	DOH IV		
CSV I		EBV I	CIH IV	FDH V	DPV II	EEH III	CKV I	DFH I	DBH I		
CSV II		CZV III	CIV IV	CZH IV	DRH I	CQH III	ENV IV	HFH II	DBV II		
CTH III		DKV V	EAV I	CZH II	DRH III	CRV II	EPH II	EDV IV	DIV V		
CTV III		DIV II	ECV I	CZV I	CZV II	CKH I	FZH I	EEV IV	GCH V		
DPH I		GDH II	CZH I	DBH II	DKV IV	CKV II	ERH IV	EMV III	FZV I		
DBV I		BRV II	CZV IV	GAH II	GEH II	DIH III	BRH IV	FVH I	HQH V		
DKV III		CXH IV	DKV I	BRH II	FVV IV	GEH I		FZV III	HQV IV		
GDV II		DGV III	ENV III	BVH II	FUH VI	ENH III			BTV III		
ECH II		BVV II	FVH V		BVH I	ENV V					
		CAV I	FVV III		DEV I	GDV III					
			ESV I			FVV V					
			BRH III			FVH IV					
			DGH I			FXH I					
			DGH III			FXH II					
			DCV I			ERH I					
						ESV III					
						BRV III					
						DDH III					
13	3	14	19	12	14	22	10	11	12	3	2

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longitudinal growth during three consecutive time periods Further injections had shown an increasing indefiniteness of line identification in the microscopical sections because of reabsorption and remodelling of the bone trabeculae of the metaphysis (Fig 1) The doses of oxytetracycline was 1 0—1 5 mg/kg body-weight being without toxic effect on growth in length (*Hansson* 1967) The gas exposures were made in defined time relation to the oxytetracycline injections (Fig 2 and 3) Within half an hour after the fourth injection the animals were killed by intravenous injection of Evipan® (Bayer) about 100 mg/kg body weight The left proximal tibia was removed chosen because of its high growth rate in combination with the comparetively flat shape of its epiphyseal growth plate (*Hansson* 1967) For this investigation of changes in growth during exposure

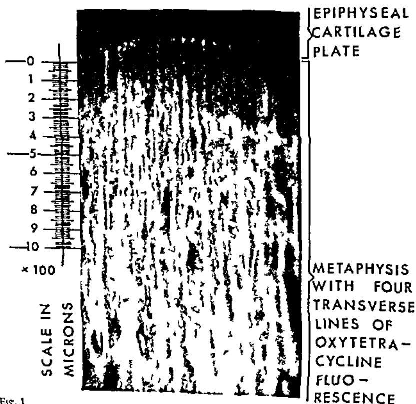


Fig. 1

Proximal tibial metaphysis of growing rabbit Microphotograph in ultraviolet fluorescence Oxytetracycline labelling of growth at intervals of 24 hrs Measuring scale showing the magnification

positive correlation which was highly significant in three age groups and *insignificant in eight* age groups When the groups were put together as listed below in 5 day groups it was significant in all the groups implying a greater daily growth in length at a higher weight

Age in days	Number	r value	t value
26—30	116	0 39	$4\ 53^{\times\times\times}$
31—35	93	0 32	$3\ 21^{\times\times}$
36—40	28	0 78	$6\ 32^{\times\times\times}$
total	237	0 17	$2\ 64^{\times\times}$

It is notable that the significance of correlation in the total material is smaller than in any of the age groups, which means that a negative factor *increases* by the fact that an older animal growths less than a younger after the age of 30 days (Fig 15) It vas assumed that the day of birth was not noted by the breeder with a higher accuracy than one or two days This made it reasonable to use the 5 day groups above The demonstrated correlation between weight and growth in this material was not of consequence in the present study, because this was based on differences in growth between consecutive days in the same animal, and with littermates in test and control groups These were made with an approximately even distribution of weights

Method for measuring of growth

The reasons for selecting the intravital oxytetracycline labelling method for this investigation are mentioned in the beginning of this chapter Since the discovery by *Andre* (1956) that tetracyclines are deposited in bone tissue this has been further studied by *Milch* et al (1958) The method was used for lamellar bone growth measurements only (see *Hansson* 1967) until it was shown that tetracyclines were deposited in the border between the metaphysis and the growth plate marking the endochondral longitudinal bone growth as well *(Hulth & Olerud* 1962) These possibilities were developed and used by *Hansson* (1964 and 1967) also reviewing the earlier literature In this investigation the oxytetracycline technic has been used as described below according to *Hansson*

The rabbits were given oxytetracycline (Terramycin® Pfitzer) intravenously in a marginal ear vein 4 times each, at intervals of 24 hrs ± 5 minutes In a smaller part of the investigation the injections were given with intervals of 12 hrs, ± 2 5 minutes These four injections allowed the determination of

longitudinal growth during three consecutive time periods Further injections had shown an increasing indefiniteness of line identification in the microscopical sections because of reabsorption and remodelling of the bone trabeculae of the m taphysis (Fig 1) The doses of oxytetracycline was 1 0—1 5 mg/kg body weight being without toxic effect on growth in length (*Hansson* 1967) The gas exposures were made in defined time relation to the oxytetracycline injections (Fig 2 and 3) Within half an hour after the fourth injection the animals were killed by intravenous injection of Evipan® (Bayer) about 100 mg/kg body weight The left proximal tibia was removed chosen because of its high growth rate in combination with the comparatively flat shape of its epiphyseal growth plate (*Hansson* 1967) For this investigation of changes in growth during exposure

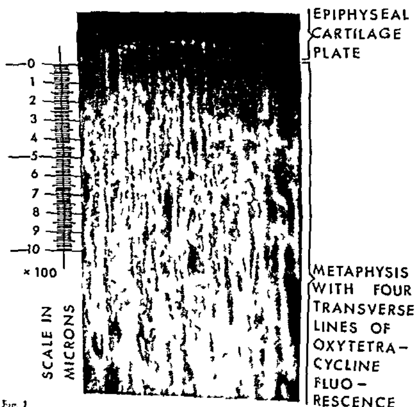


Fig. 1

P oximal t bi l metaphys s of growing rabbit Microphotograph in ul r violet fluorescence Oxytet acycline l velling of growth at intervals of 24 hrs Measuring scale showing the magnification

of the whole animal to alteration of respiratory gas tensions no important advantage could be expected by utilizing more than one epiphyseal growth region The piece of bone was fixed in concentrated ethanolum (99 5 per cent) for 12—72 hrs The bony epiphysis was then horisontally divided near the growth plate and the diaphysis was sawed off as well about 5 mm distal to the plate The resulting piece was sagitally cut in one lateral and one medial half, of which the lateral was used for sectioning Parallel to the metaphyseal trabeculae seen in the sagital cut surface the anterior quarter was cut off with a razor blade knife and the posterior quarter was used In the new surface, the cut was again controlled or adjusted parallel to the planes of the trabeculae of the metaphysis on both the surfaces exposed Further cutting of bone sections with the razor blade knife were made parallel to the trabecular system The cutting was then made in the sagital plane and about 10 sections were taken and put into Xylol for 5—10 minutes The thickness was occasionally checked and ranged between 60—120 microns as measured with a micrometer screw gauge Between 6 and 10 sections were then mounted in liquid DePeX (Gurr) on glass and covered with glass After drying in darkness the sections were examined in an ultraviolet (mercury lamp OSRAM HBO 200 W) fluorescence microscope (Zeiss) with a dark field condensor (NA 0 65/0 85) and measured with a calibrated ocular (12 5×), the objective being 10 × The primary filters used were BG 12/4+BG 38/2 5 and the secondary filter 53 With this equipment the longitudinal growth rate was measured as three distances between the metaphyseal borders of the four lines in such a way that the readings were always made with the measuring scale projected along unbroken bone trabeculae in positions where they were nearly at right angles to the growth cartilage plate (Fig 1) The error of this method has been determined earlier by side comparisons (*Hansson* 1967 *Persson* 1967 *Sunden* 1967) One or two readings were made on each section and all together about 5—10 readings were made The arithmetic mean number of readings in each animal was 7 3 in the entire material To be accepted readings should be possible along the same trabecula for all the three consecutive time periods used For the further calculations the arithmetic means of these readings were used, giving in microns the longitudinal growth rates of the proximal tibial metaphysis during three consecutive periods of time The first period before the gas treatment gave one control value to which the following growth changes could be referred A second type of growth control value was achieved by using about half of each litter as a reference group simultaneously treated with air only This gave a measure of possible growth effects caused by stress factors from change in housing and handling during the day of gas treatment and secondly it allowed for possibilities of double blind readings during microscopy with decodification of the identification numbers on the glasses made after the measuring

Statistical methods

The statistical analysis was based on differences in growth between each of the three consecutive time periods measured in the same animal In the group of animals where pure oxygen was tested it was specially analysed whether the statistical result was influenced by the fact that rounded figures were used in this investigation The mean value of the readings in each animal at each time period was rounded off 466 was put to 470 for instance This was done because the measuring stab of the microscope did give only two figures (Fig 1) The analysis demonstrated that the statistical significances were uninfluenced by this measure For each step of the investigation about 10—20 animals were exposed identically with a certain test gas and about the same number of animals to air as a control In this way it was possible to follow the changes in growth within each animal after a certain exposure and after the air exposure and then to compare the differences of effects in the two samples In the bottoms of each table given in the chapters on results the arithmetic mean of growth in each time period is given as well as the mean difference between two consecutive time periods the standard deviation of these differences the t value with degrees of significance (Student s test) and the n value

$$\text{standard deviation} = \sqrt{\frac{1}{n-1}\sum_{i=1}^{n}(X-m)^2}$$

$$t\ \text{value} = \frac{m_d-\mu_d}{\frac{S_d}{\sqrt{n}}} \quad \text{with } n-1 \text{ degrees of freedom}$$

The two sided alternative hypothesis was used in the Student s test as the direction of a possible change in growth could not be predicted The test within the material of each table is given in its bottom but the tests between control groups and the test gas groups that is between two different tables are given in the corresponding text in each chapter For this comparison the following test function was used again with a two-sided alternative hypothesis

$$t = \frac{m_x - m_y - (\mu_x - \mu_y)}{S\sqrt{\frac{1}{n_x}+\frac{1}{n_y}}} \quad \text{with } n_x+n_y-2 \text{ degrees of freedom}$$

It was tested that the variables of the samples were normally or approximately normally distributed which is required for the test It is also necessary that

the standard deviations of the populations are the same, which was tested by the function $F = \frac{S_x^2}{S_y^2}$ with $n_x - 1$ respectively $n_y - 1$ degrees of freedom In some parts of the material this was not the case and then a non parametric test was used, namely Wilcoxon s rank sum test (T), or Mann Whitney s test (U) In these cases T or U is written in the corresponding text

In the interpretation of the results conventional probability levels have been used with the following symbols written

—	$p > 0\,05$	(not significant)
×	$0\,01 < p < 0\,05$	(almost significant)
××	$0\,001 < p < 0\,01$	(significant)
×××	$p < 0\,001$	(highly significant)

Abbreviations

$\sum_{i=1}^{n} X_i$	=the um of the values of the observations (from 1 to n)
n	=the number of observations
x	=the individual observation in one time period
y	=the observation in the following time period of the same individual
x_i	=the series of individual observations from 1 to n
m	=the arithmetic mean of the observations
m_d	=the arithmetic mean of differences x—y in the sample
μ_d	=the arithmetic mean in the population of x—y
S_d	=standard deviation of the sample of the difference x—y
m_x	=the arithmet c mean of the sample for the variable x
m_y	=the arithmetic mean of the sample for the variable y
μ_x	=the arithmetic mean of the population for the variable x
μ_y	=the arithmetic mean of the population for the variable y
n_x	=the number of observations in the sample for the variable x
n_y	=the number of observations in the sample for the variable y
S_x	=standard deviation of the sample for the variable x
S_y	=standard deviation of the sample for the variable y
S	=the weighed standard deviation of the samples for the variables x and y
t	=t distribution according to Student
F	=F distribution (Dixon & Massey 1957)
T	=the rank sum according to Wilcoxon s test (— —)
U	=value in the U test according to Mann Whitney (— —)
p	=probability level

Method for change of gas tensions

With the aim of analysing the effects on growth in length during change in oxygen and carbon dioxide tensions a method was preferred which was not immobilizing and not traumatic to the bone and simple enough for the long series necessary The most convenient seemed to be to house the animals for a defined period in chambers where they could breathe the gases to be tested.

When the animals were to be exposed to the different breathing gases they were placed in either of two boxes one for the gas to be tested and one for the air as control Five to ten animals could be housed in each of the boxes measuring 60×35×35 cm The litters were divided between the boxes as listed in the tables of the following chapters The gases were supplied to the boxes through rubber tubes from standard gas cylinders The gas cylinders were delivered by Syrgas AB Alfax Malmo Sweden with the gases purified for medical use The gas mixtures were made with an accuracy of ±0 3 per cent and tested by the manufacturer (Orsat ~ analysis) On three occasions as an additional control it was also checked at the Laboratory of Aviation and Naval Medicine Institute of Physiology In a Scholander apparatus the deviations from the ordered concentrations were not more than 0 1—0 2 per cent. This department also delivered the cylinders with compressed air for the controls At the Pressure Chamber Laboratory of this institute the gas exposures were also carried out The boxes housing the animals were placed in the hyper or hypobaric chamber where the desired pressure was reached in a couple of minutes Thus there were two methods of changing the gas tensions that is by change in gas concentrations of the cylinders and by variation in the barometric pressure of the chambers The gas cylinders had a volume of 40 or 50 liters and a starting pressure between 150 and 200 kp/cm² By calculating the volume and the change in pressure it was possible to estimate the flow from the cylinders to the boxes The flow was controlled by means of an orifice through which gas was supplied at adjustable feeding pressure from the reducing valve (Aga, Sweden) on the cylinder This flow had been calibrated with a Douglas bag in the pressure chamber at the actual working pressures (manometers NAF Sweden) and the volume was later measured in a standard wet gas meter outside the chamber These precautions about the flow rate of gases were taken because it was necessary to use a flow rate big enough to wash out the carbon dioxide produced by the animals during the 8 hrs of treatment The flow was let out of the boxes after passage through holes in the lid The ventilation needed was calculated to be 400 liters/kg bodyweight of animals per hour as follows The maximal CO concentration which could be tolerated as harmless was supposed to be equivalent to 0 5 per cent at 1 atm abs i e 0 25 per cent at 2 atm abs. The production of CO_2 is not more than equal to the consumption of oxygen, that is about 0 8 liters/kg/hr (Dittmer & Grebe 1958) This was rounded to

1 0 liter/kg/hr at 1 atm abs If the CO_2 production was 1 0 liter/kg/hr and 0 25 per cent could be tolerated the flow must be 400 liters/kg/hr, i e 6 7 liters/min per kg of animal The actual flow used was between 400 and 800 liters/kg/hr checked continously as mentioned above On two occations it was also checked by Scholander analysis of the gas leaving the boxes The calculations were verified This flow through the boxes also gave a homogenisation of gases within the boxes further made certain by an extra increase in flow at the beginning of each exposure Finally the flow prevented an increase of the temperature of the boxes because of the gas temperature decrease during the gas expansion The temperature was occasionally recorded and found to be between 20 and 26°C within the boxes The humidity of the air from the cylinders was close to 0 but the animals were given water freely in an open cup Temperature, humidity, light, draught and noise were equal in the test and control hutches The lids of the hutches were transparent allowing free inspection through the windows of the pressure chamber Further details on concentrations and pressures of the tested gases are given in the chapters on results

Periods of time for change in gas tensions and for measuring of growth

The oxygen exposures should be short enough to avoid the oxygen toxicity, which is proportional both to the time and the partial pressure (*Bean* 1945) At the same time the exposures had to be long enough to allow an accurate calculation of the growth in length The method chosen allows labelling with 12 hrs intervals (*Persson* 1968) Shorter intervals seem to lead to increased difficulties in separation of the line frontiers in the microscopic sections Thus the periods of growth labelling should not be shorter than 12 hrs but to allow sufficient time for transport of the animals to and from the place of treatment and time for the intravenous injections as well 8 hrs of treatment was considered to be convenient A longer time would have limited the possible pressure of oxygen used because of toxicity This toxicity is of two major types One acute form of toxicity attects the central nervous system (*Bert* 1878) and is seen at higher tensions of oxygen that is about 3 atm abs and more The second type is the pulmonary toxicity (*Smith* 1899) which can be elicited at oxygen pressures over 0 6 atm abs during extended treatments (*Barach* 1926) With increasing partial pressures of oxygen the time for this lung damage to evolve is progressively decreased These problems are well known in humans and experimental animals (*Bean* 1945 1964 *Gerschman* et al 1964) and hold for the rabbit as well (*Binger* et al 1927) This reduces the possible advantage of using longer periods of exposure and consequently it was decided in this investigation

to use a time of treatment of 8 hrs *Treatment given in intervals for instance* of 2+2+2 hrs as in clinical praxis, reduces toxicity but has the disadvantage of masking effects in case of diphasic responses (Persson 1967) and was therefore *not used in this investigation* The treatment was used only once in each animal *be ause a repetit on for several days would have led to another two important* draw backs that is acclimatisation effets on haematopoesis (*Altland & Highman* 1952 *Brooksby* et al 1966) and secondly it would have reduced the possibilities of analysing the time lags between the treatments and the changes in growth rate

The relation between the time periods and the 8 hrs of treatment used in this *investigation is illustrated in* Fig 2 and Fig 3 *for the 24 and the 12 hrs systems used respectively As mentioned earlier only three consecutive periods of* growth were measured in each animal The maturing time of the cartilage cells from the layer of the reserve cells to the layer of degenerating and calcifying cells has been *determined* to be 2—4 days (*Messier & Leblond 1960 Kember* 1960) and it was evidently necessary to observe the possible effects on growth for 4—5 days after the treatment This problem was solved by using three consecutive *series of animals, overlapping each other with one day for the coupling together* making possible analysis of changes in growth for an extended time This is also illustrated in Fig 2 Figures 2 and 3 also illustrate that the gas treatment was given almost until the end of the period O The time lag between the end of *treatment* and the following injection for tetracycline labelling of growth was less than 1 hr in series with 24 hrs periods and half an hour in series with 12 hrs periods The reason for this was *that there could be expected to be some withdrawal effects af er the treatments In this way* it was *possible to localize immediate effe ts* and immediate withdrawal effects on different sides of the labelling lines and they were not allowed to compensate

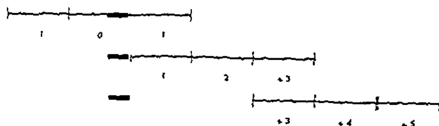


Figure 2

The time relation between the three periods of 24 hrs used for the longitudinal growth measurements in each animal and the 8 hrs of treatment given during the period named 0 and the overlapping in time between each series allowing 7 consecutive periods of 24 hrs to be compared

time for injection of oxytetracycline

▬ = *time of exposure to test gases*

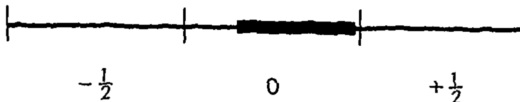


Figure 3

The time relation between the three periods of 12 hrs used for the longitudinal growth measurements in each animal and the 8 hrs of treatment given during the period named 0 The other periods are named — ½ and +½ respectively to distinguish from other series where periods of 24 hrs were used

| = *time for injection of oxytetracycline*

▬ = *time of exposure to test gases*

each other within the same period in case of diphasic effects on the growth rate (*Persson* 1967) The reasons given in this text for not using more than 8 hrs of treatment do not apply to later testing of decreased oxygen and increased carbon dioxide tensions, as the toxicity factors are not at all the same Anyhow it was decided to use the same system of periods to allow for better possibilities for comparisons of the sensitivity of growth to the different test gases tried

It was considered to be unimportant at which time in the day the injections were given as long as it was at the same time each day For practical reasons they were given between 16 30 and 17 00 with the numbered animals in a constant order The ordinary time for injection was less than one minute for each animal and each litter was begun with at a constant time each day, making the time factor equal in tests and controls This holds for the entire material where periods of 24 hrs were used When periods of 12 hrs were used the treatment was started at 11 00 and ended at 19 00 and the injections were given before 19 30 thereby marking the end of period 0 On the next morning the last injection of tetracycline was given before 07 30 that is after another 12 hrs exactly for each animal again with the animals in a constant order In this case the time chosen for injection could be of some importance if there were a diurnal variation in growth rate, as suggested by *Simmons & Nichols* (1966) This possibility has been separately studied (*Persson* 1968) but no significant variation was found However as long as the investigation is carried out as a comparison between tests and controls this possible factor is equalized

Physical and Physiological data

As a background to the description of the results obtained some basic data from respiratory physiology will be recapitulated Air constains 20 95 vol per cent of oxygen 79 02 vol per cent of nitrogen and 0 03 vol per cent of carbon dioxide

(*Dittmer & Grebe* 1958) The percentage of nitrogen given includes 0 95 vol per cent of inert gases At a barometric pressure of 760 mm Hg in dry air this means an oxygen partial pressure of 158 mm Hg Inspired into the alveoli the gas tension of oxygen has been reduced to just a little above 100 mm Hg because of the occurrence of water vapor and carbon dioxide being about 47 and 40 mm Hg respectively From the alveolar air oxygen diffuses readily over to blood In the capillary blood of the lungs pO is close to the alveolar gas tension but it will be reduced by venous admixture corresponding to the ventilation/perfusion ratio and the resulting arterial oxygen tension is about 94 mm Hg In the peripherial capillary beds this oxygen tension is reduced to 40 mm Hg in the venous blood returning to the lungs In blood oxygen is carried in two ways i e combined with haemoglobin and in physical solution The special affinity of oxygen for haemoglobin makes the arterial saturation to be about 97 per cent at the normal pO_2 of 94 mm Hg Each gram of haemoglobin can combine with 1 34 ml of oxygen and if the normal haemoglobin content is 15 g per cent this means that the haemoglobin in blood carries about 20 ml of oxygen per 100 ml blood under normal circumstances Meanwhile the amount of oxygen in physical solution is about 0 3 ml/100 ml As this physical solution has a linear relation to the gas tension in the gaseous phase it means that giving 100 per cent of oxygen in the respiratory air the pO in the arterial blood will be about 673 mm Hg increasing the oxygen content by 2 2 vol per cent of which 1 7 vol per cent is in physical solution (*Linehan* 1964) This means that an increase in tension of oxygen by 6 7 times increases the carrying capacity about 11 per cent This moderate increase in capacity is however combined with a considerable increase in the diffusion pressure The cited figures hold approximately for the rabbit as well (Chapter 7)

When the environmental barometric pressure is changed by means of a pressure chamber (Chapter 3) the gas tension of oxygen will be altered simultaneously If the pressure is raised to 2 atm abs (atm abs = atmospheres absolute = 760 mm Hg) that is 1520 mm Hg the oxygen tension in air will be about 304 mm Hg If the animals are breathing pure and dry oxygen at the same pressure the oxygen partial pressure will be 1520 mm Hg and the oxygen content in the blood will be increased from about 20 ml/100 ml to about 25 2 ml 100 ml

In Chapter 4 the results will be given of decreased oxygen tensions by the means of a hypobaric chamber that is a pressure tank where the barometric pressure can be reduced by vacuum pumps The same principles applies to this that is for instance if the pressure is reduced to half that is from 760 to 380 mm Hg the oxygen partial pressure will be reduced from 158 to 79 mm Hg if there is no water vapor At 6000 meters altitude the barometric pressure is about 354 mm Hg the oxygen partial pressure about 76 mm Hg and the alveolar oxygen tension about 35 mm Hg the alveolar carbon dioxide tension finally

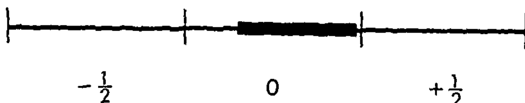


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is about 30 mm Hg, compared to 40 at sea level (*Luft* 1961) This oxygen tension corresponds to an oxygen saturation of the haemoglobin of about 68 per cent, which means that the oxygen carrying capacity per 100 ml of blood has been reduced from 20 to about 13 6 vol per cent The oxygen lack causes a hyperventilation, which reduces the alveolar carbon dioxide tension At 5000 meters the alveolar oxygen tension still according to *Luft* (1961), is about 42 mm Hg, at 4000 meters it is about 51 mm Hg at 3000 meters it is about 62 mm Hg and the alveolar carbon dioxide tension is then about 36 mm Hg

In Chapter 6 the investigation of increased carbon dioxide tension in air will be described When the normal carbon dioxide tension is raised from about 0 04 vol per cent to 3 vol per cent the alveolar carbon dioxide tension increases from about 45 5 to 47 5 mm Hg At 5 vol per cent of carbon dioxide in air the alveolar tension is about 49 5 mm Hg, and at 7 vol per cent finally, the alveolar carbon dioxide tension is about 58 mm Hg in humans (*Barcroft & Margaria* 1931 *Patterson* et al 1955) At this carbon dioxide tension the ventilation rate had increased from about 12 to about 80 liters/min and it was about the highest carbon dioxide tension that could be tolerated by the healthy test subjects After 18 hrs in about 4 per cent carbon dioxide in air the ventilation is still about 200 per cent of the normal (*Dittmer & Grebe* 1958) After 15—20 min of 3 5 per cent carbon dioxide breathing in 16 humans the jugular venous pH in blood had decreased from a mean of 7 35 to 7 32 and the arterial pH had decreased from 7 39 to 7 35 (*Patterson* et al 1955)

After this short presentation of some basic figures, illustrating important principles from the respiratory physiology the results obtained by testing the effects on longitudinal bone growth from short time alterations of respiratory gases as specified later, will be described

CHAPTER 3

RESULTS OF INCREASED OXYGEN TENSIONS

The preliminary studies of the effects on growth during increased respiratory oxygen tension for 2+2+2 hrs with *100 per cent oxygen at 2 atm abs* during one day earlier referred to had indicated an increased growth in length during the exposure followed by a depression the day after On the basis of these results the following questions were considered for further studies

Does omitting of the pauses in the intermittent oxygen exposure disclose a growth acceleration of significant magnitude earlier hidden by a diphasic effect between the periods of hyperoxygenation and the pauses between?

Does an observation extended in time after the oxygen exposure reveal later effects which can be related to younger maturing stages of the cartilage cells which may not reach the calcification zone until after a couple of days?

Does there exist a dose response relationship between effects on growth and *the oxygen tension used during the 8 hrs of treatment?*

This part of the investigation comprises a total of 193 rabbits 102 treated with increased tensions of oxygen and 91 litter mates treated simultaneously with air for control The oxygen when said to be 100 per cent pure contained less than 0 5 per cent inert gases which can be ignored. They are a part of the air also and they have no proved biological function The results are given under four headings below named A—D The percentage of oxygen in the gas mixtures conducted through the boxes, *is specified* and the ambient pressure is given in atm abs The pressure specified means the normal ambient pressure for the day of the experiment and under A another 1 atm abs *achieved by raising* the pressure this amount in the hyperbaric chamber where the boxes were stationed. The barometric pressure on the days of treatment varied *only* between 745—770 mm Hg which was not compensated for During the 8 hrs of hyperbaric oxygenation under A, the pressure in the chamber was allowed to vary ± 0 1 atm abs at most, which *means* ± *5 per cent.*

is about 30 mm Hg compared to 40 at sea level (*Luft* 1961) This oxygen tension corresponds to an oxygen saturation of the haemoglobin of about 68 per cent, which means that the oxygen carrying capacity per 100 ml of blood has been reduced from 20 to about 13 6 vol per cent The oxygen lack causes a hyperventilation which reduces the alveolar carbon dioxide tension At 5000 meters the alveolar oxygen tension still according to *Luft* (1961) is about 42 mm Hg, at 4000 meters it is about 51 mm Hg, at 3000 meters it is about 62 mm Hg and the alveolar carbon dioxide tension is then about 36 mm Hg

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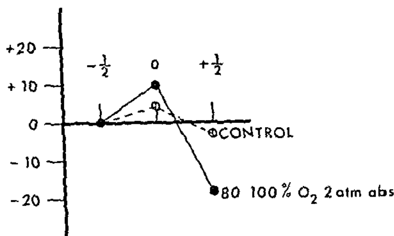


Figure 4

Mean growth changes in microns between three consecutive time periods of 12 hrs The oxygen group was treated in 80 or 100 % of O_2 at 2 atm.abs for 8 hrs during period 0 the control group simultaneously treated with air at the same pressure

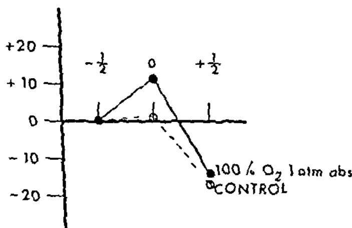


Figure 5

Mean growth changes in microns between three consecutive time periods of 12 hrs The oxygen group was treated in 100 % O_2 at 1 atm abs for 8 hrs during period 0 the control group simultaneously treated with air at the same pressure

A 80 and 100 per cent oxygen at 2 atm abs with growth recording periods of 12 hrs

This experimental series was intended to answer the first question if omitting of the treatment pauses *earlier tried*, would disclose a significant change in growth, hitherto covered *as being diphasic within the growth period measured*. Pure oxygen at 2 atm abs was first tried, but turned out to be over the limit of toxicity for the treatment of 8 hrs used *Therefore 80* per cent oxygen was tried for the same time and the *same pressure* that is an oxygen pressure of 1 6 atm abs In the first group 2 animals out *of 7* died of respiratory failure soon after the end of exposure, and in the second group 2 of 13 died with the same symtoms In both cases it was animals in the same litter that reacted in this *way and another* 5 animals (not excluded) in these two litters showed symptoms of respiratory distress but survived the measuring period The post *mortem examination* of the lungs disclosed macroscopic hepatisation, i e alveolar *exsudation* blood engorgement and haemorrhages as described by *Lorrain Smith* (1899) in 11 out of 18 rabbits treated with 80 or 100 per cent oxygen for 8 hrs In *three of the cases the* changes were slight as also in one of the controls Microscopic examination was not made as these changes have *been thoroughly* studied (*Smith* 1899) As toxicity reactions occurred in both *groups* it was considered to be justified to add them together for the statistical evaluation The arithmetic mean of the changes seemed to be the same as well *and the* figures are given in Table 2 and 3 The effects on growth is illustrated in Fig 4 as alteration of mean differences between consecutive time periods The mean values given in Tables 2—3 show an increase in growth *during period* 0 of 4 per cent in the oxygen group compared to 2 per cent in the control and a decrease during period $+^1/_2$ of 12 per cent in the oxygen group compared to 3 *per cent* in the control The statistical comparison between changes in test and control eliminates the significance of the stimulation observed during hyperoxygenation ($-^1/ \rightarrow 0$ $t=1\ 35^-$) but shows a significant decrease in growth *for the* oxygen group during the 12 hrs after the treatment ($0 \rightarrow +^1/_2$ $U=2\ 60^{\times\times}$) Because of the toxicity *reactions* observed *these exposures* were not continued The changes observed are illustrated in Fig 4

As the sensitivity of the measuring method was not expected to allow shorter observations it was necessary to lower the partial pressure of oxygen used and 100 per cent at 1 atm abs was therefore chosen *being simpler to handle* than 80 per cent oxygen at 2 atm abs

Table 3

Control animals for Table 2 Air breathing at 2 atm.abs for 8 hrs Longitudinal growth rates in microns during three successive periods of 12 hrs (−1/2 0 +1/2)

Animal	−1/2	0	+1/2
OV II	260	260	230
QV I	220	200	210
QV II	250	240	240
QV III	230	230	230
QV IV	280	290	260
RV I	280	280	260
RV II	260	250	240
RV III	250	260	250
RV IV	300	290	280
TV I	270	280	270
TV II	240	250	270
TV III	230	260	260
UV I	250	270	280
UV IV	260	260	250
VV II	230	230	230
VV III	210	230	210
Mean growth	251	255	248

Statistical analysis of differences in growth between the consecutive periods above

	−1/2 → 0	0 → +1/2
Mean diff	+4	−7
Stand. dev	13 10	14 01
t value	+1 15−	−1 96−
n value	16	16

Table 2

Increased oxygen tension by exposure to 80 and 100 per cent oxygen at 2 atm abs in hyperbaric chamber for 8 hrs during period 0 Longitudinal growth rates in microns during three successive periods of 12 hrs (—1/2 0 +1/2)

Animal	—1/	0	+1/2
TH I	250	280	240
TH II	240	280	270
TH III	260	250	280
TH IV	230	240	220
UH I	270	270	250
UH II	260	280	260
UH III	270	280	280
UH IV	250	250	240
UV II	260	270	270
UV III	250	250	240
VH II	250	250	170
VH IV	220	240	190
VV I	230	230	170
OH I	280	290	260
OH II	260	290	220
OH III	260	280	240
QH I	240	230	180
QH II	230	230	200
Mean growth	251	261	232

Statistical analysis of differences in growth between the consecutive periods above

	—1/ → 0	0 → +1/2
Mean diff	+10	—28
Stand dev	14 14	27 49
t value	+3 0××	—4 38×××
n value	18	18

B 100 per cent oxygen at 1 atm abs with growth recording periods of 12 hrs

This part describes the immediate effects up to 12 hrs after the end of the *exposure to 100 per cent oxygen at 1 atm abs* No animals died or developed respiratory distress Only one animal showed traces of the pulmonary hepatisation observed in A Consequently this partial pressure of oxygen is about the highest tolerable for 8 hrs in young rabbits Individual values and mean values of growth rates are given in Tables 4 and 5 The changes are further illustrated in Fig 5 as mean differences in test and control The mean values given in Tables 4 and 5 show an increase in growth during period 0 of 5 per cent in test compared to 0 per cent in control and a decrease in growth during period +½ of 11 *per cent in test compared to 7 per cent in control Statisti*cally the first change is significant ($t=2\,86^{\times\times}$) the second in insignificant ($t=1\,56^{-}$)

This part B had given a determination *of the highest tolerable doses of oxy*gen for 8 hrs and shown that the increase in growth earlier not significant was statistically reliable It was now necessary to illuminate on the second question whether an observation of growth extended in time after the therapy would disclose further changes referable to different stages of the cartilage cell development This demanded an observation time of 5 days (*Messier and Leblond* 1960) after the exposure with a hyperoxygenation of 100 per cent at 1 atm abs as determined to be the highest dose which could be tolerated

C 100 per cent oxygen at 1 atm abs with growth recording periods of 24 hrs

With the partial pressure of oxygen and time of exposure identical with that in part B it was considered to be justified for this prolonged observation to change the growth recording periods from 12 to 24 hrs as the earlier effects wery already determined This would allow an easier handling in respect of time consumption and give a reduced relative error of measurements which was supposed to outweight the possible advantage of using 12 hrs as the period for *the study For changes in growth* occuring later in time than 12 hrs after the gas exposure it could be presumed to be a reaction flattened out in time, thereby making it sufficient to extend the periods in use to 24 hrs In the preliminary investigation (*Persson 1967*) *the 24 hrs period* had also been used

The test groups were given 100 per cent of oxygen at 1 atm abs for 8 hrs during period 0 the controls simultaneously exposed to air from gas cylinders

Table 4

Increased oxygen tension by exposure to 100 per cent oxygen at 1 atm abs for 8 hrs during period 0 Longitudinal growth rates in microns during three successive periods of 12 hrs (−½ 0 +½)

Animal	−½	0	+½
SH I	270	290	270
SH II	280	290	280
SH III	280	290	250
XH I	240	230	2[illegible]
XH II	210	220	2[illegible]0
XH III	210	200	200
XV I	170	190	180
ADH I	270	290	250
ADH II	280	3[illegible]0	260
ADH III	280	3[illegible]0	250
ADV I	3[illegible]0	3[illegible]0	260
EVH I	230	[illegible]5[illegible]	210
EVH IV	240	270	210
EVV I	250	250	[illegible]0
EXH I	260	280	240
EXH II	240	250	210
EXV II	260	280	240
EYH I	290	29[illegible]	280
EYH III	280	270	250
EYV I	270	290	24[illegible]
FRV I	1[illegible]0	180	140
FRV II	160	180	150
FSH II	190	210	[illegible]0
FSH III	190	190	180
FSV I	160	170	170
FSV II	180	190	180
FTH I	260	280	240
FTH II	2[illegible]0	25	230
FTH IV	250	2[illegible]0	230
FTV II	210	[illegible]	200
FU I	[illegible]10	210	210
FU III	170	190	170
Mean growth	233	245	219

Statistical analysis of differences in growth between the consecutive periods above

	−½→0	0→+½
Mean diff	+12	−26
Stand dev	13 7	1[illegible] 57
t value	+4 75×××	−8 36×××
n value	32	32

Table 5

Control animals for Table 4 Air breathing at 1 atm abs for 8 hrs Longitudinal growth rates in microns during three successive periods of 12 hrs (—¹/ 0 +¹/)

Animal	—¹/	0	+¹/
SV I	300	300	280
SV II	280	270	250
XV II	230	240	240
XV III	220	220	210
ADV II	310	310	270
ADV III	290	300	250
EVH II	250	250	220
EVH III	250	250	220
EVH V	250	280	230
EVV IV	260	260	250
EXH III	260	260	230
EXV I	240	280	220
EYH II	280	280	270
EYV II	280	290	260
EYV III	300	290	260
FRH I	200	210	200
FSH I	210	210	210
FSH IV	210	200	200
FSV III	190	200	190
FSV IV	170	170	190
FTH III	260	250	250
FTV I	240	240	240
FTV III	270	250	220
FU II	250	240	240
FU IV	220	210	200
FU V	220	220	200
Mean growth	248	249	231

Statistical analysis of differences in growth between the consecutive periods above

	—¹ → 0	0 → +¹
Mean diff	+2	—18
Stand dev	12 55	18 91
t value	+0 637	—4 98
n value	26	26

The results are given in Tables 6 and 7 showing in comparison a significant increase of 3 per cent between period —1 and period 0 (t=3 42××) The continued observation for 5 periods of 24 hrs after period 0 did not reveal any statistically significant alteration in the continued growth rate of the metaphysis with comparison between test and control (0 → +1 t=0 23⁻ +1 → +2 t=0 19⁻ +2 → +3 t=0 04⁻ +3 → +4 t=1 24⁻ +4 → +5 t=0 89⁻) This is illustrated in Fig 6 This does *not* however indicate that the growth in test and control was the same after the end of the oxygen treatment From the statistical point of view on the contrary it means that the acceleration of growth observed during the treatment with 100 per cent of oxygen continued as a growth rate on a little higher level than in the control group It might be that the growth stimulation subsided slowly and extended over serveral periods after the treatment making each step so small that the method did not allow measuring of the changes The recorded stimulation was 3 per cent and the error of the method is 1—2 per cent (*Hansson* 1967 *Persson* 1967) which makes this possibility probable To evaluate this and to answer the question as to when the stimulation ends the absolute values of growth were compared This is made in Fig 7 as a quotation of the mean value of growth in the test with that in the control group for the same day The growth in the test group is thereby expressed as a percentage of the control for each day In this way the overlapping groups in period +1 and +3 *respectively* were utilized by summing which makes the samples larger on these two days This comparison indicated that the stimulation subsided from +4 per cent to 1 per cent from period +2 to +4 (Fig 7)

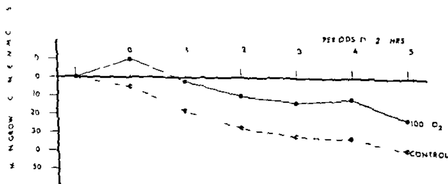


Figure 6

Longitudinal growth of the proximal tibial metaphysis in rabbits at increased oxygen tension by exposure to 100 % of oxygen at 1 atm.abs for 8 hrs during period 0 Growth recordings by oxytetracycline labelling for 7 consecutive time periods of 24 hrs Mean growth changes in microns form day to day measured within the same animal Figures made continous by overlapping observations in period +1 and +3

Table 5

Control animals for Table 4 Air breathing at 1 atm abs for 8 hrs Longitudinal growth rates in microns during three successive periods of 12 hrs (—½ 0 +½)

Animal	—½	0	+½
SV I	300	300	280
SV II	280	270	250
XV II	230	240	240
XV III	220	220	210
ADV II	310	310	270
ADV III	290	300	250
EVH II	250	250	220
EVH III	250	250	220
EVH V	250	280	230
EVV IV	260	260	250
EXH III	260	260	230
EXV I	240	280	220
EYH II	280	280	270
EYV II	280	290	260
EYV III	300	290	260
FRH I	200	210	200
FSH I	210	210	210
FSH IV	210	200	200
FSV III	190	200	190
FSV IV	170	170	190
FTH III	260	250	250
FTV I	240	240	240
FTV III	270	250	220
FU II	250	240	240
FU IV	220	210	200
FU V	220	220	200
Mean growth	248	249	231

Statistical analysis of differences in growth between the consecutive periods above

	—½ → 0	0 → +½
Mean diff	+2	—18
Stand dev	12 55	18 91
t value	+0 63	—4 98
n value	26	26

Table 7

Control animals for Table 6 Air breathing at 1 atm.abs for 8 hrs Longitudinal growth rates in microns during successive periods of 24 hrs (−1 0 +1 +2 +3 +4 +5) in three overlapping series of animals

Animal	−1	0	+1	Animal	+1	+2	+3	Animal	+3	+4	+5
DYH II	520	570	510	EDH I	410	410	410	EFH II	420	470	440
DYV I	550	550	540	EDH II	370	370	380	EFV I	500	500	490
DYV II	530	530	510	EDV I	430	440	450	EFV II	520	520	520
DZH I	500	500	500	EDV III	460	460	450	EFV IV	490	480	470
DZH IV	540	530	510	EDV V	390	390	380	EGH II	490	490	470
DZV I	510	530	480	EEH II	410	410	440	EGV I	520	510	500
DZV III	430	430	430	EEH V	370	280	310	EGV III	520	530	500
DZV V	490	510	5 0	EEV V	390	360	350	EHH I	520	530	530
DZV VI	460	490	450	EJH III	490	440	390	EHH III	530	540	540
GTH III	450	4 0	440	EKH III	470	470	460	EHH IV	500	490	490
GTH IV	430	490	490	EKV I	470	470	480	EHV III	510	5 0	500
GTV II	430	410	400	EL II	510	510	500				
GTV IX	45	440	430	EMH II	530	530	510				
GUH III	530	510	490	EMH IV	540	520	510				
GUV III	5 0	490	480	EMH V	590	580	580				
GV II	570	510	500	EMV IV	540	530	500				
GV III	510	5 0	490	EMV IX	490	490	490				
GV V	530	510	490								
GXH I	510	490	470								
GXV II	540	530	5 0								
GXV III	53	520	500								
Mean growth	[illegible]1	496	48		459	451	446		502	501	49[illegible]

Statistical analysis of differences in growth between the consecutive periods above

	−1 → 0	→ 1	1 → 2	2 → 3	3 → 4	4 → 5
Mean diff	−5	−13	−9	−4	−1	−6
Stand d	14 70	14 76	16 54	19 70	8.31	13 65
t value	−1 63−	−4 8×××	−2.20×	−0 86−	−0.36−	−1.55−
n value	21	21	17	17	11	11

Table 6

Increased oxygen tension by exposure to 100 per cent oxygen at 1 atm abs for 8 hrs during period 0. Longitudinal growth rates in microns during successive periods of 24 hrs (−1, 0, +1, +2, +3, +4, +5) in three overlapping series of animals

Animal	−1	0	+1	Animal	+1	+2	+3	Animal	+3	+4	+5
DYH I	550	550	540	EDH III	400	400	410	EFH I	470	460	450
DYH III	540	550	530	EDH IV	470	470	480	EFH III	440	450	420
DYH IV	540	540	540	EDH V	450	450	430	EFH IV	500	500	470
DYH V	500	510	480	EDV III	420	410	410	EFV III	510	510	510
DYV IV	530	520	520	EEH I	390	400	410	EGH I	490	490	490
DZH II	510	520	510	EEH IV	420	420	420	EGH III	510	510	500
DZH III	480	500	470	EEH VI	430	430	440	EGH IV	520	520	510
DZH IV	540	530	510	EJH I	500	480	480	EGV II	510	530	510
DZH V	520	510	500	EJH II	510	490	470	EHH II	500	510	500
DZV II	*510*	*500*	*510*	*EKH II*	*520*	*500*	*510*	*EHH V*	*550*	*550*	*540*
DZV IV	510	510	490	EKV II	540	530	500	EHV I	500	500	490
GTH I	500	500	500	EKV III	520	500	460	EHV II	540	550	550
GTH II	450	470	480	EL I	450	430	400	EHV IV	470	470	460
GTV I	410	440	440	EMH I	530	500	490				
GUH II	510	550	530	EMH III	500	490	500				
GUV I	500	520	490	EMH VI	450	490	510				
GUV II	520	540	530	EMV I	570	540	540				
GV I	500	510	500	EMV II	520	520	520				
GV IV	490	510	480								
GXH II	540	560	540								
GXH III	510	530	520								
Mean growth	508	518	505		477	469	466		501	504	492

Statistical analysis of differences in growth between the consecutive periods above

	−1 → 0	0 → 1	1 → 2	2 → 3	3 → 4	4 → 5
Mean diff	+10	−12	−8	−4	+3	−11
Stand dev	14.14	12.61	16.65	17.20	7.51	10.77
t value	+3.24××	−4.50×××	−1.98−	−0.96−	+1.48−	−3.61××
n value	21	21	18	18	13	13

Table 7

Control animals for Table 6 Air breathing at 1 atm abs for 8 hrs Longitudinal growth rates in microns during successive periods of 24 hrs (−1 0 +1 +2 +3 +4 +5) in three overlapping series of animals

Animal	−1	0	+1	Animal	+1	+2	+3	Animal	+3	+4	+5
DYH II	570	520	510	EDH I	410	410	410	EFH II	420	420	440
DYV I	550	550	540	EDH II	370	370	380	EFV I	500	500	480
DYV II	53	530	510	EDV I	430	440	450	EFV II	520	520	520
DZH I	500	500	500	EDV III	460	460	450	EFV IV	490	480	470
DZH IV	540	530	510	EDV V	390	390	380	EGH II	490	490	470
DZV I	510	530	480	EEH II	410	410	440	EGV I	520	510	500
DZV III	430	430	430	EEH V	320	280	310	EGV III	5 0	530	500
DZV V	490	510	5 0	EEV V	390	360	350	EHH I	520	530	530
DZV VI	460	49	450	EJH III	490	440	390	EHH III	530	540	540
GTH III	450	420	440	EKH III	470	470	460	EHH IV	5 0	490	490
GTH IV	490	490	490	EKV I	470	470	480	EHV III	510	500	500
GTV II	430	410	4 0	EL II	510	510	500				
GTV IV	450	440	430	EMH II	530	530	510				
GUH III	530	510	490	EMH IV	540	520	510				
GUV III	5 0	49	480	EMH V	590	580	580				
GV II	57	510	500	EMV IV	540	530	5 0				
GV III	510	5 0	490	EMV IV	490	490	490				
GV V	530	510	490								
GXH I	510	490	470								
GXV II	54	530	520								
GXV III	530	5 0	500								
Mean growth	5 1	496	482		459	451	446		502	5 1	495

Statistical analysis of differences in growth between the consecutive periods above

	−1 → 0	0 → 1	1 → 2	2 → 3	3 → 4	4 → 5
Mean diff	−5	−13	−9	−4	−1	−6
Stand d	24.70	24.76	26.54	19.70	8.31	13.65
t value	−1.63−	−4.28×××	−2.20×	−0.86−	−0.36−	−1.55−
n value	21	21	17	17	11	11

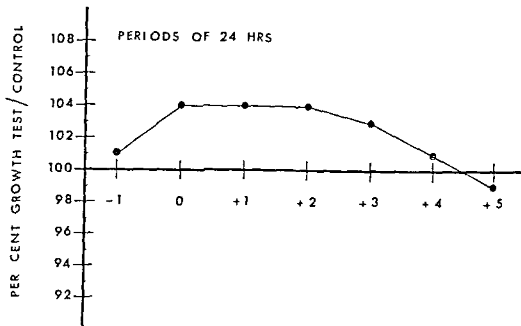


Figure 7

Per cent growth in length from the proximal tibial growth plate of rabbits treated with 100 % O_2 at 1 atm abs for 8 hrs during period 0 compared to control groups of littermates simultaneously treated with air from gas cylinders

As the gases tried might influence the respiration and because of the fact that rabbits regulate their heat by panting instead of sweating some attention had to be paid to the *temperature factor* In testing 100 per cent of oxygen at 1 atm abs for 8 hrs the rectal temperatures were measured with a mercury thermometer in 14 animals before and within a minute after the exposure They ranged between 38 0 and 39 5°C but there was no difference between tests and controls This is in accordance with *Valenzuela* (1877) The temperature of the two boxes was also the same at the end of the experiment

D 100 to 21 per cent oxygen at 1 atm abs with growth recording periods of 12 hrs

A preliminary test of 80 per cent and 40 per cent of oxygen in nitrogen for 8 hrs at 1 atm abs was made in 25 animals but the effects were insignificant It was therefore considered not worth carrying on with to avoid a further splitting up of the material These values are therefore not reported in detail and

an analysis of these pressures has not been carried out because a determination of the limits of the effects was not essential for this investigation

Regarding the questions in the beginning of this chapter the following statements can be made The omitting of the intervals of the hyperbaric oxygenation earlier reported did show an influence by increased oxygen on the longitudinal growth of the metaphysis which was statistically significant An acceleration of growth starting during exposure to 100 per cent of oxygen at 1 atm abs was observed Further an extended observation for 5 days after the exposure did not reveal statistically significant changes but probably a gradual decrease in growth back to the level of the control groups during periods +3 and +4 occured (Fig 7) A dose response relationship existed so that toxicity reactions occurred when the partial pressure of oxygen was increased above 1 atm abs for 8 hrs eliminating the stimulation

After the examination of effects on growth caused by increased oxygen tensions of the respiratory air it seemed to be valuable for the interpretation to study as well the effects of reduced oxygen tensions

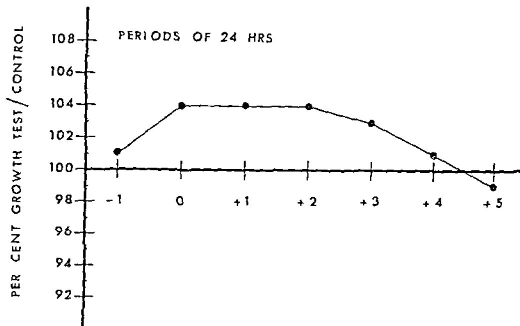


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A. Air at 3000 meters altitude with growth recording periods of 12 hrs

The experimental results are given in Table 8 to be compared with the control scale in Table 9. There was no significant effect on growth at 3000 meters (0.70 atmosphere) for the 8 hrs of exposure used. The comparison values statistically were $-\frac{1}{2} \rightarrow 0$ t = 0.90 and $0 \rightarrow +\frac{1}{2}$ t = 0.04.

Table 8

Reduced oxygen tension by exposure to 3000 meters altitude in hypobaric chamber for 8 hrs during period 0. Longitudinal growth rate in microns during successive periods of 12 hrs ($-\frac{1}{2}$, 0, $+\frac{1}{2}$)

Animal	$-\frac{1}{2}$	0	$+\frac{1}{2}$
AYII I	220	220	[illegible]
AYII II	180	160	170
AYII III	170	160	130
AYII IV	190	180	150
AYII V	180	170	160
AZV I	150	130	140
AZV II	150	150	150
AZV III	180	190	180
AZV IV	180	180	150
AZV V	180	180	160
BBII I	310	300	[illegible]
BBII II	[illegible]	310	[illegible]
BBII III	310	310	[illegible]
BBV I	[illegible]	[illegible]	[illegible]
BBV II	300	[illegible]	[illegible]
BBV III	300	290	[illegible]
BDV I	130	130	[illegible]
BDV II	140	170	130
BDV III	120	130	130
Mean growth	210	209	[illegible]

Statistical analysis of differences in growth between the consecutive periods above

	$-\frac{1}{2} \rightarrow 0$	$0 \rightarrow +\frac{1}{2}$
Mean diff	—	−8
Stand dev	33.8	14.63
t value	−0.78	−4.31*
n value	[illegible]	19

CHAPTER 4

RESULTS OF DECREASED OXYGEN TENSIONS

The simplest way to reduce the oxygen tension for groups of animals during 8 hrs seemed to be by using a hypobaric chamber It was considered indicated to begin with this method, although a lowering of the environmental pressure would reduce the partial pressure of other gases in air as well These other gases were not expected to influence the growth rates The control animals were housed outside the chamber and the test animals inside the chamber kept in an open box Pellets and water were given freely to both as always The pressure in the chamber was lowered to pressures corresponding to 3000, 4000, 5000 and 6000 meters respectively in four series Exposure and measuring times were as described in Chapter 2 (Fig 2 and 3) According to the transformation list of the station 3000 meters was equivalent to 526 mm Hg 4000 meters was 462 mm Hg, 5000 meters was 405 mm Hg and 6000 meters was equivalent to 354 mm Hg An adjustable spring loaded valve kept the pressure constant by letting in a small flow of air which increased if the pumps were about to lower the pressure too much The hypobaric chamber was cylindrical length 225 cm diameter 254 cm and this magnitude made special efforts for temperature regulation and carbon dioxide control unnecessary The results will be described in the order the experiments were performed, beginning with the moderate hypoxia accomplished by reducing the pressure to the equivalent of 3000 meters with growth recording in half days Stepwise in different series the oxygen lack was increased in simulated altitudes from 3000 to 6000 meters and after the 12 hrs series of growth recordings the same degrees of hypoxia were analysed with growth recording periods of 24 hrs for a more extended observation time This part of the investigation comprises 461 animals distributed as specified in the tables

\ Air at 3000 meters altitude with growth recording periods of 12 hrs

he experimental results are given in Table 8 to be compared with the control esult in Table 9 There was no significant effect on growth at 3000 meters 070 atm abs) for the 8 hrs of exposure used The comparison values statisti ally were $-\frac{1}{2} \rightarrow 0$ t=0 90⁻ and $0 \rightarrow +\frac{1}{2}$ t=0 04⁻

Table 8

Reduced oxygen tension by exposure to 3000 meters altitude in hypobaric chamber for 8 hrs during period 0 Longitudinal growth rate in microns during successive periods of 12 hrs ($-\frac{1}{2}$ 0 $+\frac{1}{2}$)

Animal	$-\frac{1}{2}$	0	$+\frac{1}{2}$
AYH I	220	220	200
AYH II	180	160	170
AYH III	170	160	150
AYH IV	190	180	150
AYH V	180	170	160
AZV I	150	130	140
AZV II	150	150	150
AZV III	180	190	180
AZV IV	180	180	150
AZV V	180	180	160
BBH I	310	300	3 0
BBH II	3 0	310	3 0
BBH III	310	310	3 0
BBV I	300	290	3 0
BBV II	3 0	3 0	290
BBV III	300	290	3 0
BDV I	130	130	130
BDV II	140	170	130
BDV III	120	130	130
Mean growth	210	2 8	199

Stat st cal analysis of differences in growth between the con ecu ive periods above

	$-\frac{1}{2} \rightarrow 0$	$0 \rightarrow \frac{1}{2}$
Mean diff	— 1 2	—8
Stand dev	11 8	14 63
t value	—0 78⁻	—2 51 ×
n value	19	19

Table 9

Control animals for Table 8 10 and 11 (3000—6000 meters in hypobaric chamber) resting out side the chamber for 8 hrs during period 0 Longitudinal growth rates in microns during successive periods of 12 hrs (—½ 0 +½)

Animal	—½	0	+½
YV I	220	220	210
YV II	240	250	250
YV III	250	250	230
ZV II	250	250	250
ZV III	250	250	250
AAV II	260	260	250
ACV II	280	280	260
ACV III	260	290	250
AKV II	310	300	300
AKV III	300	310	320
AKV IV	290	290	290
AKV V	280	270	260
AUV I	260	260	250
AVV I	250	260	250
BBH IV	310	310	300
BBV IV	300	290	280
BDV IV	120	110	110
Mean growth	261	262	254

Statistical analysis of differences in growth between the consecutive periods above

	—½ → 0	0 → ½
Mean diff	+1	—8
Stand dev	9 93	11 31
t value	+0 39ⁿˢ	—3 00××
n value	17	17

B Air at 4000 meters altitude with growth recording periode of 12 hrs

The influences on growth at 4000 meters (0 61 atm abs) are given in Table 10 to be compared with the control values in Table 9 There is an almost significant *decrease in growth in comparison between the period before the treatment and* the period of treatment and this significance is unaltered in comparison with the control group (−½ → 0 t=2 57× 0 → +½ t=0 51⁻)

Table 10

Reduced oxygen tension by exposure to 4000 meters altitude in hypobaric chamber for 8 hrs during period 0 Longitudinal growth rates in microns during successive periods of 12 hrs (−½ 0 +½)

Animal	−½	0	+½
AUH I	290	280	270
AUH II	80	280	240
AUH III	290	270	260
AUH IV	290	290	260
AUV II	240	230	240
AUV III	290	270	250
AVH I	230	210	270
AVH II	240	250	250
AVH III	280	270	250
AVV II	260	250	250
Mean growth	269	260	249

Statistical analysis of differences in growth between the consecutive periods above

	−½ → 0	0 → ½
Mean diff	−9	−11
Stand dev	9 94	16 63
t value	−2 86	−[illegible] 09⁻
lb	10	10

Table 9

Control animals for Table 8 10 and 11 (3000—6000 meters in hypobaric chamber) resting out side the chamber for 8 hrs during period 0 Longitudinal growth rates in microns during successive periods of 12 hrs (—1/ 0 +1/)

Animal	—1/	0	+1/
YV I	220	220	210
YV II	240	250	250
YV III	250	250	230
ZV II	250	250	250
ZV III	250	250	250
AAV II	260	260	250
ACV II	280	280	260
ACV III	260	290	250
AKV II	310	300	300
AKV III	300	310	320
AKV IV	290	290	290
AKV V	280	270	260
AUV I	260	260	250
AVV I	250	260	250
BBH IV	310	310	300
BBV IV	300	290	280
BDV IV	120	110	110
Mean growth	261	262	254

Statistical analysis of differences in growth between the consecutive periods above

	—1/ → 0	0 → 1/2
Mean diff	+1	—8
Stand dev	9 93	11 31
t value	+0 39—	—3 00××
n value	17	17

Table 12

Reduced oxygen tension by exposure to 60 0 meters altitude in hypobaric chamber for 8 hrs during period 0 Longitudinal growth rates in microns during successive periods of 12 hrs (—1/2 0 +1/2)

Animal	—1/2	0	+1/2
ZH I	240	220	220
ZH II	240	[illegible]	[illegible]
ZH III	270	230	230
ZH IV	240	230	[illegible]
ZV I	230	220	220
AAH I	260	260	210
AAH II	250	230	220
AAV I	260	250	220
ACH I	270	250	240
ACH II	270	270	230
ACH III	280	250	240
ACV I	260	240	240
Mean growth	256	238	224

Statistical analysis of differences in growth between the consecutive periods above

	—1/2 → 0	0 → 1/2
Mean diff	—18	—13
Stand dev	13 37	17 25
t value	—4 74 ××	—2 68×
n value	12	12

D Air at 6000 meters altitude with growth recording periods of 12 hrs

The results of testing growth at a simulated altitude of 6000 meters (0 47 atm abs) are given in Table 12 to be compared with the control values in Table 9 There is a decrease in mean growth of 7 per cent in comparison between the day before and the day of treatment and a further decrease of another 5 per cent to the day *after* The first decrease is highly significant also compared to the controls (—1/2 → 0 t=4.52××× 0 → +1/2 t=0 96⁻)

C Air at 5000 meters altitude with growth recording periods of 12 hrs

The results of testing growth at 5000 meters (0 54 atm abs) are given in Table 11 to be compared with the control animals in Table 9 The differences are statistically insignificant (—½ → 0 t=1 13⁻, 0 → +½ t=1 72⁻) in comparison between test and control animals but significant within the test group (Table 11) The direction of the changes in growth is the same as at 4000 meters

Table 11

Reduced oxygen tension by exposure to 5000 meters altitude in hypobaric chamber for 8 hrs during period 0 Longitudinal growth rates in microns during successive periods of 12 hrs (—½ 0 +½)

Animal	—½	0	+½
YH I	230	230	230
YH II	270	270	240
YH III	240	240	240
YH IV	240	250	200
YH V	220	220	230
YV IV	240	240	230
AKH I	290	290	280
AKH II	280	280	260
AKH III	310	320	300
AKH IV	310	300	260
AKH V	310	290	260
AKV V	300	270	260
Mean growth	*270*	*267*	*249*

Statistical analysis of differences in growth between the consecutive periods above

	—½ → 0	0 → ½
Mean diff	—3	—18
Stand dev	11 55	17 65
n value	—1 00⁻	—3 43
t value	12	12

Table 14

Control animals for Tables 13 15 16 and 17 (3000—6000 meters in hypobaric chamber) resting out side the chamber for 8 hrs during period 0 Longitudinal growth rates in microns during successive periods of 24 hrs (—1 0 +1 +2 +3 +4 +5) in three overlapping series of animals

Animal	—1	0	+1	Animal	+1	+2	+3	Animal	+3	+4	+5
CEH III	530	530	490	ALV II	540	550	550	BAH V	480	470	44
CEV I	530	530	520	ALV III	510	510	510	BCV I	550	550	540
CFH I	510	570	520	AIV IV	580	590	560	BEH III	460	450	450
CFH III	540	540	540	AMV II	560	550	550	BEH IV	510	5 0	480
CFV I	54	550	560	AMV III	6 0	610	590	BGV II	380	330	370
CFV IV	520	5 0	510	AMV IV	590	590	580	BGV III	340	340	330
CGH I	510	510	500	ANV III	510	540	530	BGV IV	350	350	330
CGH III	580	580	570	ANV IV	560	550	550	BHV III	450	450	450
CGV II	550	550	550	AOV II	490	490	490	BJV IV	370	470	380
CGV III	550	550	530	AOV III	490	480	460	BJV V	250	240	240
CGV IV	560	560	560	APH V	490	470	5 0	BKH III	530	530	510
CPH IV	470	470	450	ARV V	550	550	550	BKV I	600	6 0	590
CPV II	5 0	570	570	ASH III	340	350	3 0	BKV II	580	560	530
CPV III	470	470	470	ASH IV	370	380	380	BLH III	590	6 0	590
CPV IV	460	460	460	ATH III	340	340	33	BLV I	570	560	560
CQH II	550	550	550	ATH IV	350	360	350	BLV II	490	49	490
CQV I	520	52	520	AXH VI	4 0	380	390	BNV II	560	550	550
CQV III	560	560	54					BNV III	580	570	560
CRH I	490	490	490					BOV III	610	600	60
CRH III	510	5 0	49					BOV IV	550	560	550
CRV I	520	570	520								
CRV III	5 0	5 0	470								
CHH II	540	540	5 0								
CHH IV	550	540	530								
CHV I	520	5 0	5 0								
CJH I	5 0	520	5 0								
CKV III	550	54	5 0								
CLH IV	550	540	540								
CLV I	550	550	540								
CLV IV	570	570	5								
CLV VI	490	480	470								
CMH I	600	6 0	6 0								
CNH I	480	490	490								
CNV II	580	590	550								
COH I	560	560	550								
COH III	6 0	670	590								
CSH II	55	550	5 0								
CSH III	550	570	5								
CVS III	450	430	4 0								
CTH II	570	550	55								
CTH IV	510	540	510								
CUH I	550	5 0	450								
CUH III	510	510	510								
CUV II	530	530	5 0								
CUV III	57	550	5								
Mean growth	534	529	514		489	488	484		490	488	475

This part of the investigation (A—D) had shown that there was a decreased growth in length during air breathing at reduced barometric pressure, persisting during the first 12 hrs. after the exposure. The changes are highly significant only at 6000 meters altitude. The next step was to follow these effects for an extended period after the treatment. On the same grounds as given in Chapter 6 measuring periods of 24 hrs. were used for the continued study. This is given below (E—H).

E. Air at 3000 meters altitude with growth recording periods of 24 hrs

The results of these exposures to air at 3000 meters (0.70 atm abs.) for 8 hrs are given in Table 13 to be compared to the controls in Table 14. There are no significant effect at this comparison even during this extended observation for 5 days after the end of treatment.

Table 13

Reduced oxygen tension by exposure to 3000 meters altitude in hypobaric chamber for 8 hrs. during period 0. Longitudinal growth rates in microns during successive periods of 24 hrs (−1, 0, +1, +2, +3, +4, +5) in three overlapping series of animals

Animal	−1	0	+1	Animal	+1	+2	+3	Animal	+3	+4	+5
CEH I	540	540	500	AXH I	390	380	370	BAH I	490	450	420
CEH II	530	530	510	AXH II	390	390	380	BAH II	450	450	440
CEH IV	540	540	510	AXH III	310	310	310	BAH III	490	490	450
CFH II	520	510	500	AXH IV	220	220	220	BAH IV	530	520	500
CFH IV	530	530	500	AXH V	260	260	270	BAV I	440	440	430
CFV II	510	530	510	AXV I	370	400	350	BAV II	500	490	480
CFV III	520	520	510	AXV II	320	330	370	BAV III	570	560	560
CGH II	540	540	540	AXV III	340	340	340	BAV IV	480	490	480
CGH IV	530	520	520	AXV IV	370	380	370	BC I	520	520	520
CGH V	500	500	490					BC II	550	550	550
CGV I	510	510	530					BC III	540	530	520
CGV V	530	540	500					BC IV	540	540	510
Mean growth	525	526	510		330	334	331		512	507	492

Statistical analysis of differences in growth between the consecutive periods above

	−1 → 0	0 → 1	1 → 2	2 → 3	3 → 4	4 → 5
Mean diff.	+1	−16	+4	−3	−5	−15
Stand. dev.	7.93	17.82	11.30	23.45	11.98	13.91
t value	$+0.36^{-}$	$-3.07^{\times}$	$+1.18^{-}$	-0.43^{-}	-1.62^{-}	$-3.79^{\times\times}$
n value	12	12	9	9	12	12

Table 14

Control animals for Tables 13 15 16 and 17 (3 00—6000 meters in hypobaric chamber) resting out side the chamber for 8 hrs during period 0 Longitudinal growth rates in microns during successive periods of 24 hrs (−1 0 +1 +2 +3 +4 +5) in three overlapping series of animals

Animal	−1	0	+1
CEH III	530	530	490
CEV I	530	530	520
CFH I	510	[illegible]	520
CFH III	540	540	540
CFV I	540	[illegible]	560
CFV IV	520	[illegible]	510
CGH I	510	510	[illegible]
CGH III	590	590	570
CGV II	550	550	550
CGV III	550	550	530
CGV IV	560	560	560
CPH IV	470	470	450
CPV II	[illegible]	[illegible]	[illegible]
CPV III	470	470	470
CPV IV	460	460	460
CQH II	550	550	550
CQV I	[illegible]	520	520
CQV III	560	560	540
CRH I	490	490	490
CRH III	510	[illegible]	490
CRV I	[illegible]	520	520
CRV III	[illegible]	[illegible]	470
CHH II	540	540	500
CHH IV	550	540	530
CHV I	[illegible]	[illegible]	500
CJH I	520	520	[illegible]
CKV III	550	540	[illegible]
CLH IV	550	540	[illegible]
CLV I	550	550	540
CLV IV	570	570	[illegible]
CLV VI	[illegible]	480	470
CMH I	600	600	[illegible]
CNH I	[illegible]	490	490
CNV II	580	590	550
COH I	560	560	550
COH III	[illegible]	[illegible]	590
CSH II	550	550	[illegible]
CSH III	550	[illegible]	[illegible]
CVS III	450	430	[illegible]
CTH II	570	[illegible]	[illegible]
CTH IV	560	540	510
CUH I	550	[illegible]	450
CUH III	510	510	510
CUV II	550	530	520
CUV III	[illegible]	550	[illegible]
Mean growth	534	529	514

Animal	+1	+2	+3
ALV II	540	550	550
ALV III	510	510	510
ALV IV	580	590	560
AMV II	560	550	550
AMV III	620	610	590
AMV IV	590	590	580
ANV III	530	540	530
ANV IV	560	550	550
AOV II	490	490	490
AOV III	490	480	460
APH V	490	470	[illegible]
ARV V	550	550	550
ASH III	340	350	350
ASH IV	370	380	380
ATH III	340	340	330
ATH IV	350	360	350
AXH VI	[illegible]	380	[illegible]
Mean growth	489	488	484

Animal	+3	+4	+5
BAH V	480	470	440
BCV I	550	550	540
BEH III	460	450	450
BEH IV	510	500	480
BGV II	380	380	370
BGV III	340	340	330
BGV IV	350	350	330
BHV III	450	450	450
BJV IV	370	400	380
BJV V	250	240	240
BKH III	530	530	510
BKV I	600	600	590
BKV II	580	[illegible]	530
BLH III	590	600	590
BLV I	570	560	560
BLV II	490	490	490
BNV II	560	[illegible]	[illegible]
BNV III	580	570	560
BOV III	610	600	560
BOV IV	550	560	550
Mean growth	490	488	475

Table 14 continued

Statistical analysis of differences in growth between the consecutive periods above

	−1 → 0	0 → 1	1 → 2	2 → 3	3 → 4	4 → 5
Mean diff	—4	—15	—1	—4	—3	—13
Stand dev	10 35	18 42	10 54	13 26	10 70	11 64
t value	—2 88ˣˣ	—5 50ˣˣˣ	—0 46⁻	—1 28⁻	—1 04⁻	—4 80ˣˣˣ
n value	45	45	17	17	20	20

F Air at 4000 meters altitude with growth recording periods of 24 hrs

The results of studying growth during air breathing at 4000 meters (0 61 atm abs) for 8 hrs are given in Table 15 to be compared to the control values in

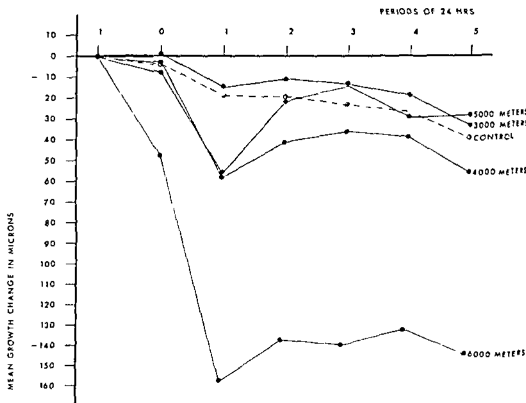


Figure 8

Longitudinal growth of the proximal tibial metaphysis in rabbits at reduced oxygen tension by exposure to simulated altitudes of 3000 4000 5000 and 6000 meters for 8 hrs during period 0 Growth recordings by oxytetracycline labelling for 7 consecutive time periods of 24 hrs Mean growth changes in microns from day to day measured within the same animal Figures made continous by overlapping observations in period +1 and +3

Table 14 This comparison shows a highly significant decrease in growth from the day of exposure to the day after (t=5 97×××) and further by a return towards normal as a highly significant increase between period +1 and +2 (t=4 61×××) The first decrease is about 11 per cent the following increase about 5 per cent between periods +1 and +2 There is a further increase of 2 per cent between periods +2 and +3 (t=1 92⁻) The effects are illustrated in Fig 8 After period +3 there are no significant changes (+3 → +4 t=0 13⁻ +4 → +5 t=1 01⁻)

Table 15

Reduced oxygen tension by exposure to 4000 meters altitude in hypobaric chamber for 8 hrs during period 0 Longitudinal growth rates in microns during successive periods of 24 hrs (−1 0 +1 +2 +3 +4 +5) in three overlapping series of animals

Animal	−1	0	+1	Animal	+1	+2	+3	Animal	+3	+4	+5
CPH I	00	5 0	460	ASH I	3 0	320	310	BEH I	470	470	460
CPH II	470	470	450	ASH II	320	330	330	BEH II	490	480	480
CPH III	490	490	440	ASV I	310	340	350	BGH I	380	370	370
CPV I	490	5 0	450	ASV II	350	3 0	360	BGH II	380	370	330
CQH I	5 0	510	430	ASV III	270	290	310	BGH III	4 [illegible]	39[illegible]	360
CQH IV	570	560	510	ASV IV	310	340	340	BGH IV	410	420	370
CQV II	540	540	460	ATH I	360	370	380	BGV I	370	370	360
CRH II	5[illegible]0	5 0	430	ATH II	300	310	31[illegible]	BJV I	350	350	340
CRH IV	490	470	410	ATV I	290	290	320	BJV II	350	360	330
				ATV II	3[illegible]0	350	35[illegible]	BJV III	3 [illegible]	3 0	320
				ATV III	350	360	360				
				ATV IV	3 0	310	320				
Mean growth	5 8	5 4	449		315	33[illegible]	337		392	390	372

Statistical analysis of differences in growth between the consecutive periods above

	−1 → 0	0 → 1	1 → 2	2 → 3	3 → 4	4 → 5
Mean diff	−3	−56	+17	+5	−2	−18
Stand dev	8 66	19 44	9 85	11 68	7 89	18 14
t value	−1 15⁻	−8 57×××	+5 86×××	+1 48⁻	−0 80⁻	−3 14×
n value	9	9	12	1[illegible]	10	10

Table 14 continued

Statistical analysis of differences in growth between the consecutive periods above

	—1 → 0	0 → 1	1 → 2	2 → 3	3 → 4	4 → 5
Mean diff	—4	—15	—1	—4	—3	—13
Stand dev	10 35	18 42	10 54	13 26	10 70	11 64
t value	—2 88××	—5 50×××	—0 46⁻	—1 28⁻	—1 04⁻	—4 80×××
n value	45	45	17	17	20	20

F Air at 4000 meters altitude with growth recording periods of 24 hrs

The results of studying growth during air breathing at 4000 meters (0 61 atm abs) for 8 hrs are given in Table 15 to be compared to the control values in

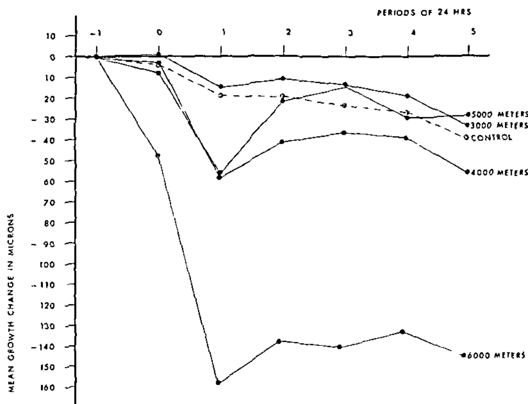


Figure 8

Longitudinal growth of the proximal tibial metaphysis in rabbits at reduced oxygen tension by exposure to simulated altitudes of 3000 4000 5000 and 6000 meters for 8 hrs during period 0 Growth recordings by oxytetracycline labelling for 7 consecutive time periods of 24 hrs Mean growth changes in microns from day to day measured within the same animal Figures made continous by overlapping observations in period +1 and +3

and period +1 there was a highly significant decrease (U=4 08$^{\times\times\times}$) measuring 11 per cent in mean value After this there was a highly significant increase in growth (U=4 48$^{\times\times\times}$) between period +1 and period +2 measuring 6 per cent The following days showed no significant changes between consecutive days in the test group but in the control group there was a significant decrease in growth of unknown cause during the last day (Table 14)

H Air at 6000 meters altitude with growth recording periods of 24 hrs

The results of studying growth at 6000 meters (0 47 atm abs) for 8 hrs are given in Table 17 with controls in Table 14 At this altitude a comparison of the groups showed a highly significant decrease in growth already between period −1 and the period of exposure (0) measuring 9 per cent (T=33 5$^{\times\times\times}$) The earlier observed decrease given in part D is verified and followed by a further decrease the day after treatment of anothr 20 per cent now highly significant (T=23 5$^{\times\times\times}$) The increase between period +1 and +2 observed at 4000 and 5000 meters is still significant at 6000 meters (U=2 92$^{\times\times}$) in spite of the pronounced reduction observed during the first two periods at this altitude During period +2 and until +5 there is still no significant delayed change in growth in comparison between tests and controls (+2 → +3 U=0 43 +3 → +4 t=2 02^{-} +4 → +5 t=0 05^{-}) Many animals seemed to regain a normal growth during these days (Table 17) but the mean change does not fully compensate for the decreased growth in the first days (Fig 8)

As pronounced effects had been observed at the altitudes studied it was considered to be of no value to proceed further as the hypoxia if further increased would severely influence on the general condition of the animals which was not the intention The growth reactions described in A—H were caused by reduced barometric pressure and it was considered necessary to investigate if the same changes could be induced by a reduction of the oxygen concentration alone at a normal barometric pressure This was necessary not only to exclude other factors of the hypobaric condition used which might influence on growth but also to prepare the way for the investigation of the importance of the carbon dioxide pressure because reduction of the oxygen tension induces a hyperventilation which gives a hypocapnia The first step was to try 1? per cent of oxygen at normal pressure corresponding to about 4500 meters of altitude in air breathing

G Air at 5000 meters altitude with growth recording periods of 24 hrs

This study of the effects on growth at exposure to 5000 meters (0 54 atm abs) for 8 hrs is descripted in Table 16, with the control animals listed in Table 14 A comparison between the two materials showed no immediate effect at exposure (—1 → 0 t=1 50⁻) but with comparison of changes between period 0

Table 16

Reduced oxygen tension by exposure to 5000 meters altitude in hypobaric chamber for 8 hrs during period 0 Longitudinal growth rates in microns during successive periods of 24 hrs (—1 0 +1 +2 +3 +4 +5) in three overlapping series of animals

Animal	—1	0	+1	Animal	+1	+2	+3	Animal	+3	+4	+5
CHH I	490	490	420	ALH I	480	500	510	BHH I	350	350	360
CHH III	540	530	510	ALH II	510	530	540	BHH II	390	360	360
CHV II	530	500	440	ALH III	520	530	550	BHH III	380	350	350
CHV III	520	510	500	ALV I	450	500	510	BHH IV	310	260	260
CJH III	510	510	450	AMH I	490	520	520	BHV I	420	420	420
CKH II	560	570	520	AMH II	530	570	570	BHV II	350	350	350
CKH III	550	540	510	AMH III	530	550	540	BKH I	550	530	540
CLH I	540	530	480	AMH IV	530	580	580	BKH II	480	470	460
CLH II	550	520	510	AMV I	530	540	540	BLH I	610	610	610
CLH V	530	510	460	ANH I	490	540	590	BLH II	560	550	550
CLV II	540	540	460	ANH II	500	540	540				
CLV III	570	560	530	ANH III	540	590	590				
CLV V	550	540	540	ANH IV	470	550	550				
CMH II	600	590	490	ANV I	510	550	550				
CMH III	580	570	480	ANV II	540	550	560				
CNH II	560	560	460								
CNV I	570	560	510								
COH II	560	560	490								
COH IV	570	570	560								
Mean growth	548	540	491		508	543	549		440	425	426

Statistical analysis of differences in growth between the consecutive periods above

	—1 → 0	0 → 1	1 → 2	2 → 3	3 → 4	4 → 5
Mean diff	8	—49	+35	+7	—15	+1
Stand dev	10 15	31 18	19 95	13 97	17 16	4 83
t value	—3 62××	—6 92×××	+6 73×××	+1 85⁻	—2 76×	+0 65⁻
n value	19	19	15	15	10	10

and period +1 there was a highly significant decrease ($U=4\ 08^{\times\times\times}$) measuring 11 per cent in mean value After this there was a highly significant increase in growth ($U=4\ 48^{\times\times\times}$) between period +1 and period +2 measuring 6 per cent The following days showed no significant changes between consecutive days in the test group but in the control group there was a significant decrease in growth of unknown cause during the last day (Table 14)

H Air at 6000 meters altitude with growth recording periods of 24 hrs

The results of studying growth at 6000 meters (0 47 atm abs) for 8 hrs are given in Table 17 with controls in Table 14 At this altitude a comparison of the groups showed a highly significant decrease in growth already between period −1 and the period of exposure (0) measuring 9 per cent ($T=33\ 5^{\times\times\times}$) The earlier observed decrease given in part D is verified and followed by a further decrease the day after treatment of anothr 20 per cent now highly significant ($T=23\ 5\ ^{\times\times}$) The increase between period +1 and +2 observed at 4000 and 5000 meters is still significant at 6000 meters ($U=2\ 92^{\times\times}$) in spite of the pronounced reduction observed during the first two periods at this altitude During period +2 and until +5 there is still no significant delayed change in growth in comparison between tests and controls (+2 → +3 $U=0\ 43^{-}$ +3 → +4 $t=2\ 02^{-}$ +4 → +5 $t=0\ 05^{-}$) Many animals seemed to regain a normal growth during these days (Table 17) but the mean change does not fully compensate for the decreased growth in the first days (Fig 8)

As pronounced effects had been observed at the altitudes studied it was considered to be of no value to proceed further as the hypoxia if further increased would severely influence on the general condition of the animals which was not the intention The growth reactions described in A—H were caused by reduced barometric pressure and it was considered necessary to investigate if the same changes could be induced by a reduction of the oxygen concentration alone at a normal barometric pressure This was necessary not only to exclude other factors of the hypobaric condition used which might influence on growth but also to prepare the way for the investigation of the importance of the carbon dioxide pressure because reduction of the oxygen tension induces a hyperventilation which gives a hypocapnia. The first step was to try 1 per cent of oxygen at normal pressure corresponding to about 4500 meters of altitude in air breathing

Table 17

Reduced oxygen tension by exposure to 6000 meters altitude in hypobaric chamber for 8 hrs during period 0 Longitudinal growth rates in microns during successive period of 24 hrs (—1 0 +1 +2 +3 +4 +5) in three overlapping series of animals

Animal	—1	0	+1	Animal	+1	+2	+3	Animal	+3	+4	+5
CSH IV	520	500	350	AOH I	420	480	480	BNH I	560	600	590
CTH I	530	450	310	AOH II	510	540	490	BNH II	600	610	600
CTV II	570	480	430	AOH III	460	480	450	BNH III	590	610	600
CUH II	600	550	420	AOV I	440	450	420	*BOH I*	*560*	*540*	*560*
CUH IV	530	500	410	APH I	470	480	480	BOH II	560	570	540
CUV I	570	550	440	APH II	520	510	490	BOH III	530	530	490
				APH III	400	400	440	BOH IV	550	550	530
				APH IV	*440*	*440*	*440*	*BOV I*	*510*	*520*	*510*
				APV I	460	500	520	BOV II	560	560	560
				ARV II	430	450	470				
				ARV III	420	450	460				
				ARV IV	430	460	460				
Mean growth	553	505	393		450	470	467		558	566	553

Statistical analysis of differences in growth between the consecutive periods above

	—1 → 0	0 → 1	1 → 2	2 → 3	3 → 4	4 → 5
Mean diff	—48	—112	+20	—3	+8	—12
Stand dev	*30 61*	*37 10*	*19 54*	*25 35*	*16 42*	*17 16*
t value	—3 87$^{\times}$	—7 36$^{\times\times\times}$	+3 54$^{\times\times}$	—0 45^{-}	+1 42^{-}	—2 14^{-}
n value	6	6	12	12	9	9

I Twelve per cent oxygen in nitrogen at 1 atm abs with growth recording periods of 24 hrs

Twelve per cent oxygen corresponds to about 4 500 meters altitude that is a barometric pressure of 434 mm Hg The exposure was for a duration of 8 hrs during period 0 The results are given in Table 18 with the control animals in Table 19 The statistical comparison between changes in tests and controls shows a significant decrease in growth (—6 per cent) between the period of exposure and the day after (U = 2 93$^{\times\times}$) A subsequent increase reported in part F—H is observed (Table 18) but not statistically significant (U = 1 03^{-}) The other comparisons between changes in tests and controls showed no differenses either (+1 → +2 U = 1 03^{-} +2 → +3 t = 1 02^{-} +3 → +4 U = 0 25^{-} +4 → +5 t = 1 87^{-}) It was considered to be indicated to further lower the oxygen tension

Table 18

Reduced oxygen tension by exposure to 12 per cent oxygen in nitrogen for 8 hrs during period 0. Longitudinal growth rates in microns during successive periods of 24 hrs (—1 0 +1 +2 +3 +4 +5) in three overlapping series of animals

Animal	—1	0	+1	Animal	+1	+2	+3	Animal	+3	+4	+5
DLH I	470	490	420	DKH II	440	430	440	ENH I	430	420	420
DLV I	5 0	480	430	DKH III	420	430	430	ENH IV	380	360	360
DLV II	4 0	380	350	DKH V	440	440	440	ENV I	440	420	390
DLV IV	480	490	460	DJH I	450	470	430	EOH I	440	420	380
DMH I	530	520	490	DJH IV	450	420	390	EOH IV	470	450	440
DMH II	510	490	450	DJV IV	460	460	410	EOV III	450	450	430
DMH III	500	5 0	500	GEV II	530	520	510	EPH I	460	440	460
DMH IV	480	470	460	GEV III	550	540	540	EPH III	470	470	470
DMV I	520	490	430	GFH I	460	510	470	EPH V	490	480	490
DNH I	570	560	490	GFH III	410	440	440	EPV II	440	420	400
DNH II	540	550	490	GFV I	450	530	510	EPV III	500	500	500
DNV II	530	510	460	GFV II	4 0	450	440	FCH IV	370	410	410
								FHH II	520	520	510
								FHV I	45[illegible]	380	370
								FHV II	460	450	470
								FHV IV	500	5[illegible]0	490
								FJH I	540	540	530
								FJH II	490	460	470
								FJV I	510	510	500
								FJV II	450	450	440
								FJV IV	510	5 0	510
Mean growth	5 3	489	450		455	470	454		465	455	450

Statistical analysis of differences in growth between the consecutive periods above

	—1 → 0	0 → 1	1 → 2	2 → 3	3 → 4	4 → 5
Mean diff	—14	—39	+15	—16	—10	—5
Stand dev	17 46	1 56	3[illegible] 05	19 75	19 87	15 04
t value	—3 15 ×	—7 19 ×	+1 62 –	—2 78 ×	—[illegible] 42 ×	—[illegible] 60 –
n value	1[illegible]	12	12	1[illegible]	21	21

Table 19

Control animals for Table 18 (12 per cent oxygen in nitrogen) exposed to air for 8 hrs during period 0. Longitudinal growth rates in microns during successive periods of 24 hrs (−1 0 +1 +2 +3 +4 +5) in three overlapping series of animals

Animal	−1	0	+1	Animal	+1	+2	+3	Animal	+3	+4	+5
DLH II	490	490	480	DKH I	410	450	430	ENH II	480	470	440
DLH III	520	500	500	DKH IV	460	450	460	ENH V	450	430	470
DLH IV	490	480	470	DKV II	490	490	490	ENV II	430	470	360
DLV II	500	490	480	DIH II	470	470	460	EOH II	410	410	[illegible]
DMH V	530	530	500	DIH V	460	460	440	EOH III	430	410	[illegible]
DMV II	510	520	500	DIV I	460	460	470	EOV I	490	480	430
DMV III	550	550	520	DIV III	450	450	440	EOV II	460	450	450
DMV IV	550	550	540	GEH III	470	450	430	EPH IV	510	500	490
DMV V	520	520	510	GEV I	500	500	500	EPV I	490	480	470
DNH III	550	530	520	GFH II	500	500	500	EPV IV	530	520	510
DNV I	560	560	550	GFH IV	440	430	380	FGH II	390	390	[illegible]
				GFV III	460	450	450	FGH V	400	410	410
				GFV IV	390	400	400	FHH I	500	510	490
								FHH III	490	480	[illegible]
								FHH IV	490	480	450
								FHV III	530	520	510
								FJH III	520	510	510
								FJH IV	500	490	490
								FJH V	510	510	[illegible]
								FJV III	530	520	510
Mean growth	526	523	507		456	458	450		477	469	456

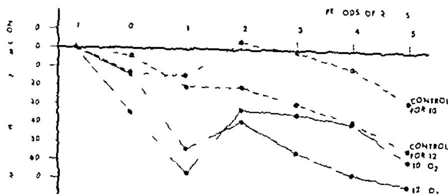
Statistical analysis of differences in growth between the consecutive periods above

	−1 → 0	0 → 1	1 → 2	2 → 3	3 → 4	4 → 5
Mean diff	−4	−16	0	−8	−9	−14
Stand dev	8 42	9 38	14 14	16 25	9 33	15 01
t value	−1 59−	−6 26×××	0	−1 88−	−4 07×××	−4 17×××
n value	11	11	13	13	20	20

K Ten per cent oxygen in nitrogen at 1 atm abs with growth recording periods of 24 hrs

Ten per cent oxygen corresponds to an altitude of about 5900 meters or a barometric pressure of 365 mm Hg The exposure was for a duration of 8 hrs as always Rabbits can survive even 8 or 7 per cent oxygen (*Binger* 1927) but

they can not keep a normal weight beyond 5500 meters (*Champbell* 1935) The results are given in Table 20 with the control animals in Table 21 The tendencies earlier described were again observed The relative changes in growth were −7 per cent during the day of exposure compared to the day before again − 7 per cent between period 0 and period +1 there after +8 per cent to period +2 A comparison of the absolute values of growth during the following periods to +5 shows that the control animals in average have a little better growth rate than the test groups which illustrates that the changes at this degree of hypoxia probably are affecting the growth for an extended time after return to normal oxygen tension This was also the case at 6000 meters earlier described The statistical comparison between changes in tests and in controls demonstrates an almost significant decrease in growth from the day before to the day of treatment (U=2 02×) and a further decrease to the day after treatment which was significant (U=2 93××) After this time there was no statistical significance in the differences between changes in test and in control up to five days after the end of the exposure to 10 per cent of oxygen compared to air (+1 → +2 t=1 21⁻ +2 → +3 t=0 09⁻ +3 → + 4 t=0 69⁻ +4 → +5 t~0 27⁻)



Figu 9

Long udinal growth of the proximal tib al metaphysis in rabbits at reduced oxygen en on by exposu e to a gas mixture with 10 and 12 of oxygen respectively in nitrogen at 1 atm abs Exposu e t me 8 hrs during period 0 Growth reco dings by oxytetra c cl ne label ng fo 7 consecut e t me pe iods of 24 h s Mean growth changes in m c ons f om d y to day measured within the same animal Figu es made continous by ove lapp ng ob ervations in period +1 and +3

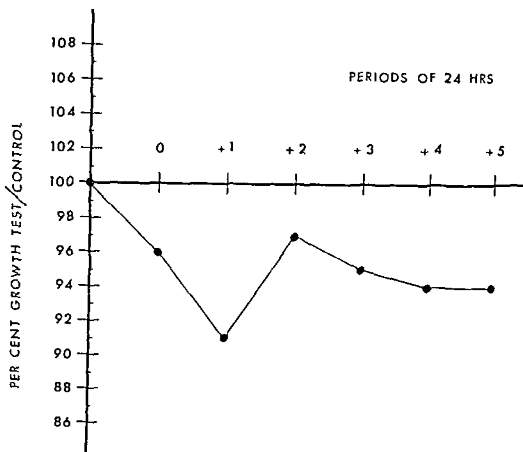


Figure 10

Per cent growth in length from the proximal tibial growth plate of rabbits treated with 10 % O in N_2 at 1 atm abs for 8 hrs during period 0 compared to control groups of litter mates simultaneously treated with air from gas cylinders

The decrease in growth during hypoxia is again observed for 24 hrs after the end of treatment (Fig 9) The increase that followed between period +1 and +2 is not statistically significant in the test of 12 and 10 per cent of oxygen reported above which it was at the test of growth during hypobaric conditions corresponding to 4000 5000 and 6000 meters altitude Looking at the absolute values of growth in the 10 per cent oxygen series however the same increase is observed during that time This is illustrated in Fig 10 where test values have been divided by the control of the same day as described in Chapter 3 for 100 per cent oxygen (Fig 7)

Table 70

Reduced oxygen tension by exposure to 10 per cent oxygen in nitrogen for 8 hrs during period 0. Longitudinal growth rates in microns during successive periods of 24 hrs (−1 0 +1 +2 +3 +4 +5) in three overlapping series of animals

Animal	−1	0	+1	Animal	+1	+2	+3	Animal	+3	+4	+5
DOH I	5 0	440	390	DSV I	440	440	440	FDH I	450	450	440
DOH II	45	430	41	DSV III	48	480	46	FDH II	460	450	450
DOV IV	5 0	480	430	DT II	510	520	530	FEH II	500	500	5 0
DPH III	470	350	260	DUV II	490	540	530	FEH III	5 0	500	490
DPH IV	46	4	430	DUV VI	5 0	550	550	FEV I	530	540	5 0
DPV III	43	370	280	DVH I	370	390	410	FFH I	470	470	440
DRH II	4 0	350	350	DVH II	320	360	420	FFH III	520	540	480
DRV I	4 0	380	350	DXV II	460	540	510	FFV II	5 0	550	530
DRV IV	410	390	380	DXV V	480	49	480	FFV IV	510	510	5 0
FAH I	48	440	390	DXV VI	440	520	480	EAH I	390	380	360
FAH III	49	480	460					EAH II	420	440	4 0
FAH V	440	4 0	360					EAH III	430	410	360
FBH I	4 0	4 0	390					EAV III	450	430	410
FBH IV	4	37	390					EAV III	450	430	410
FCH I	45	43	420					EBH I	350	340	340
FCH IV	470	470	460					EBH II	250	250	280
FCV I	5 0	5 0	470					ECV II	3 0	270	240
FCV II	530	510	510					ECV III	3 0	260	250
Mean growth	457	4 3	391		449	483	481		432	429	410

Statistical analysis of differences in growth between the consecutive periods above

	−1 → 0	0 → 1	1 → 2	2 → 3	3 → 4	4 → 5
Mean diff	−34	−3	+34	−2	−4	−19
Stand dev	7 06	3 64	3 6	8.21	18 01	21.76
t value	−5 4	−4 19	+3 51××	−0 22−	−0 81−	−3 56××
n value	18	18	10	10	17	17

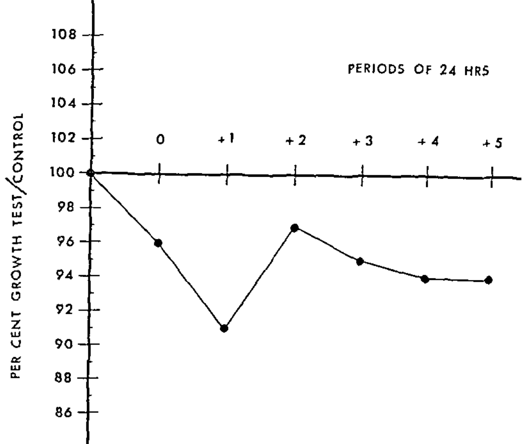


Figure 10

Per cent growth in length from the proximal tibial growth plate of rabbits treated with 10 % O_2 in N_2 at 1 atm abs for 8 hrs during period 0 compared to control groups of litter mates simultaneously treated with air from gas cylinders

The decrease in growth during hypoxia is again observed for 24 hrs after the end of treatment (Fig 9) The increase that followed between period +1 and +2 is not statistically significant in the test of 12 and 10 per cent of oxygen reported above which it was at the test of growth during hypobaric conditions corresponding to 4000 5000 and 6000 meters altitude Looking at the absolute values of growth in the 10 per cent oxygen series however the same increase is observed during that time This is illustrated in Fig 10 where test values have been divided by the control of the same day as described in Chapter 3 for 100 per cent oxygen (Fig 7)

Table 20

Reduced oxygen tension by exposure to 10 per cent oxygen in nitrogen for 8 hrs during period 0 Longitudinal growth rates in microns during successive periods of 24 hrs (—1 0 +1 +2 +3 +4 +5) in three overlapping series of animals

Animal	—1	0	+1	Animal	+1	+2	+3	Animal	+3	+4	+5
DOH I	5 0	440	390	DSV I	440	440	440	FDH I	450	450	440
DOH II	450	430	410	DSV III	480	480	460	FDH II	460	450	450
DOV IV	5 0	480	430	DT II	510	520	530	FEH II	500	540	570
DPH III	470	350	260	DUV II	490	540	530	FEH III	500	540	490
DPH IV	460	470	430	DUV VI	500	550	550	FEV I	530	540	540
DPV III	430	370	280	DVH I	370	390	410	FFH I	470	470	440
DRH II	4 0	350	350	DVH II	320	360	420	FFH III	520	540	480
DRV I	4 0	380	350	DXV II	460	540	510	FFV II	520	550	530
DRV IV	410	390	380	DXV V	480	490	480	FFV IV	510	510	500
FAH I	*48*	*440*	*390*	*DXV VI*	*440*	*520*	*480*	*EAH I*	*390*	*380*	*360*
FAH III	490	480	460					EAH II	470	440	400
FAH V	440	4 0	360					EAH III	430	410	360
FBH I	470	4 0	390					EAV III	450	430	410
FBH IV	420	370	390					EAV III	450	430	410
FCH I	450	430	420					EBH I	350	340	340
FCH IV	470	470	460					EBH II	250	250	280
FCV I	520	5 0	470					ECV II	3 0	270	240
FCV II	530	510	510					ECV III	3 0	60	250
Mean growth	457	423	391		449	483	481		432	429	410

Statistical analysis of differences in growth betaeen the consecutive periods above

	—1 → 0	0 → 1	1 → 2	2 → 3	3 → 4	4 → 5
Mean diff	—34	—37	+34	—2	—4	—19
Stand dev	27 06	32 64	30 62	28 21	18 01	21 76
t value	—[illegible] 4×××	—4 19 ×	+3 51××	—0 22—	—0 81—	—3 56××
n value	18	18	10	10	17	17

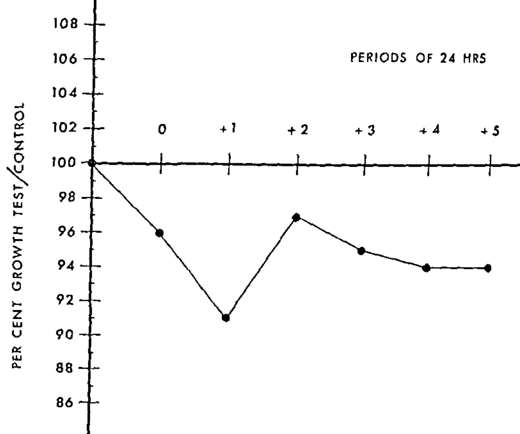


Figure 10

Per cent growth in length from the proximal tibial growth plate of rabbits treated with 10 % O_2 in N_2 at 1 atm abs for 8 hrs during period 0 compared to control groups of litter mates simultaneously treated with air from gas cylinders

The decrease in growth during hypoxia is again observed for 24 hrs after the end of treatment (Fig 9) The increase that followed between period +1 and +2 is not statistically significant in the test of 12 and 10 per cent of oxygen reported above which it was at the test of growth during hypobaric conditions corresponding to 4000 5000 and 6000 meters altitude Looking at the absolute values of growth in the 10 per cent oxygen series however the same increase is observed during that time This is illustrated in Fig 10 where test values have been divided by the control of the same day as described in Chapter 3 for 100 per cent oxygen (Fig 7)

Height of the cartilage plate after 10 per cent of oxygen for 8 hrs

It was clear that a lowering of the partial pressure of oxygen in the respiratory air did affect the growth in length of the metaphysis This influence was in a certain proportion to the degree of hypoxia induced with no changes at 3000 meter and severe changes at 6000 meters altitude for 8 hrs in unacclimatized animals The question was now whether this effect on the growth rate of the metaphysis represented a temporary shift of the calcification border or affected the total epiphyseal cartilage plate Theoretically three different possibilities existed

1 The hypoxia acted mainly in the zone of degeneration and calcification where the cartilage cells meet the blood vessels again
2 The hypoxia acted more evenly over all the maturing stages of the cartilage cells from the reserve layer to the degenerating layer
3 The hypoxia acted more in the top layers of proliferating cells than in the metaphyseal end

This question could possibly be answered by measuring of the thickness of the whole cartilage plate simultaneously with a recording of the metaphyseal growth rate by tetracycline labelling as above The same three possibilities regarding the position of the most sensitive cells presumably existed also at increased doses of oxygen earlier described but as the effects on growth observed during hyperoxia were quantitavely smaller it was considered to be advisable to study this first at a reduced oxygen pressure

If conditions agreed mostly to point one above there could be expected to be an increased height of the plate as the younger cells then should have continued the growth while the calcification border had slowed down during decreased oxygen tension as recorded at 10 per cent of oxygen in nitrogen described above in this chapter This slow down was maximal in period +1 up to 24 hrs after the end of the exposure to 10 per cent of oxygen This moment was therefore chosen for sacrifying 32 rabbits at the age generally used Half of the series was treated in low oxygen half in air The proximal tibia of one side was taken for fixation in formaline decalcified sectioned with a microtome and mounted Standard staining with haematoxylin eosin was used and the height of the cartilage plate was measured with the same optic equipment as elsewhere in this investigation The readings were made blind with decodification of tests and controls after the reading Efforts were made to measure on sections where the columns of the cells were longitudinally cut The other tibia in each animal was taken for ultraviolet microscopy of the oxytetracycline labelling made simultaneously The growth rates showed the decreases described. The statistical comparison of the height of the plate in tests and controls showed an almost significant difference the height being less in animals exposed to 10 per cent of oxygen ($t = 2.17$× 31 degrees of freedom) The differences were

Table 21

Control animals for Table 20 (10 % oxygen in nitrogen) exposed to air for 8 hrs durr period 0 Longitudinal growth rates in microns during successive periods of 24 hrs (—1 0 +1 +2 +3 +4 +5) in three overlapping series of animals

Animal	—1	0	+1	Animal	+1	+2	+3	Animal	+3	+4	+5
DOH III	470	460	450	DSH I	570	560	540	FDH III	430	430	43[illegible]
DOV II	490	490	480	DT III	500	500	500	FDH IV	440	440	4[illegible]0
DPH II	450	420	410	DUV IV	500	510	490	FEH I	550	560	550
DPV I	420	360	350	DVH III	460	490	480	FEH IV	520	500	5[illegible]0
DRV II	400	390	400	DVH IV	400	400	490	FEV II	570	570	560
DRV III	420	390	360	DVH V	500	520	490	FEV III	510	50[illegible]	490
FAH II	430	410	410	DXV II	460	540	510	FFH II	550	550	53[illegible]
FAH IV	450	450	450	DXV III	470	500	490	FFH IV	570	570	5[illegible]0
FBH II	440	420	450	DXV IV	480	480	480	FFV I	540	530	540
FBH III	410	400	400					FFV III	500	520	480
FBH V	400	400	400					EAH IV	380	340	3[illegible]
FCH II	430	430	430					EAV II	360	360	370
FCH III	520	530	530					EBH IV	370	360	350
FCV III	540	540	540					EBV III	330	310	260
FCV IV	550	540	550					ECH I	410	400	390
								ECH III	370	340	300
Mean growth	455	442	441		482	500	497		463	455	438

Statistical analysis of differences in growth between the consecutive periods abo e

	—1 → 0	0 → 1	1 → 2	2 → 3	3 → 4	4 → 5
Mean diff	—13	—1	+18	—3	—8	—17
Stand dev	*17 51*	*13 02*	*27 28*	*36 74*	*14 83*	*19 22*
t value	—2 80×	—0 40−	+1 96−	—0 27−	—2 02−	—3 51××
n value	15	15	9	9	16	16

RESULTS OF DECREASED OXYGEN TENSION COMBINED WITH INCREASED CARBON DIOXIDE TENSION

A Ten per cent oxygen plus five per cent carbon dioxide in nitrogen at 1 atm abs with growth recording periods of 24 hrs

The reason for addition of carbon dioxide to the gas with reduced oxygen tension is given in the end of Chapter 4 It was natural to continue with 10 per cent of oxygen in nitrogen because of the pronounced effects on growth observed at that concentration of oxygen The problem was to select the concentration of carbon dioxide to be added for preventing the out washing of carbon dioxide during the hyperventilation which was induced by the oxygen lack in the experiments described in Chapter 4 It was decided to use 5 per cent carbon dioxide admixture to reach an approximately normal alveolar CO tension If this concentration would give a slight accumulation of carbon dioxide instead, this factor could be separatly studied later In this part of the investigation the same technic as described in Chapter 4 was used only with the difference that the gas cylinders contained 10 per cent oxygen plus 5 per cent carbon dioxide all in nitrogen The treatment was for 8 hrs at 1 atm abs with growth recording periods of 24 hrs as earlier described

The results are given in Table 23 with the control values in Table 24 The effects are further recorded in Fig 11 as the mean differences between consecutive time periods in tests and controls separately The mean growth in the test group showed a decrease of 4 per cent from the period before treatment to the period of treatment and a further decrease of 8 per cent to the period after exposure followed by an increase in growth of 8 per cent between period +1 and +2 After this time there was no statistical difference between the changes in test and control groups The statistical comparison values were $-1 \rightarrow 0$ $U=3.68^{\times\times}$ $0 \rightarrow +1$ $U=4.40^{\times\times\times}$ $+1 \rightarrow +2$ $t=5.52^{\times\times\times}$ $+2 \rightarrow +3$ $t=0.41^{-}$ $+3 \rightarrow +4$ $t=0^{-}$ $+4 \rightarrow +5$ $t=0.95^{-}$ The degrees of freedom can be seen in Table 23 and 24

As in chapter 3 the temperature was measured to see whether the hyperventilation induced by this hypoxia had influenced on the body heat regulation In all 15 rabbits with 7 controls and 8 test animals were used for this In opposit to the increased and decreased oxygen exposures an effect was now measurable At the end of the exposure to 5 per cent carbon dioxide plus 10 per

quantitatively small. This result implies that the effect was not solely localised to the degenerating layer of the cartilage plate but to a major part. Point three was excluded by *the fact that decreases in growth were observed already during* the exposure (Fig. 9 and 10). If the height of the plate had been found to be unchanged by the hypoxia it had then been necessary to measure it immediately at the end of the exposure to rule out a possibility, that it had regained its thickness during the 24 hrs. after exposure which now were allowed to pass. There is a parallellity between the metaphyseal growth and the height of the cartilage plate in less acute experiments (*Hansson* 1967) but to limit the present work it was not carried on further, and the other experiments performed were not supplemented by this method.

At this point it was necessary to consider the possibility that the changes observed were not directly due to the reduced oxygen tension but to a *respiratory alcalosis with hypocapnia caused by the hyperventilation* which was induced by the oxygen lack. This hyperventilation did not influence on the body *temperature* as measured immediately after the exposure to a simulated altitude of 5900 meters for 8 hrs. The rectal temperatures before and after treatment showed no *differences between 7 treated animals and 5 controls. To prevent the* out-washing of carbon dioxide during the hypoxemic hyperventilation thereby keeping pCO_2 and the pH of the blood near the normal values (*Honda & Kreuzer* 1966) it was decided to add a certain dose of carbon dioxide to the gas with reduced oxygen content. The aim was to *see whether this CO addition* would change the effects of the hypoxia described above.

Table 24

Control an ma's for T ble 23 (10 pe cent oxygen plus 5 per cent carbon dioxide in nitrogen) Exposed to air for 8 hrs during period 0 Longi udinal growth rates in microns during successive periods of 24 hrs (—1 0 +1 +2 +3 +4 +5) in three overlapping series of animals

Animal	—1	0	+1	Animal	+1	+2	+3	Animal	+3	+4	+5
GBH III	450	420	440	FVH III	450	450	45?	FYH III	450	450	460
GBH IV	*440*	*440*	*440*	*FVV IV*	*3?0*	*350*	*350*	*FYH IV*	5?0	490	460
GCH IV	410	470	430	FXH V	540	530	530	FYV III	470	490	470
GCV I	410	410	410	FXV II	550	550	550	FYV IV	490	480	480
GCV III	440	430	450	FXV III	530	520	520	FZH II	440	430	420
GCV IV	480	480	480	FXV IV	550	540	540	FZH III	390	380	390
GDH IV	450	450	440	GGH I	490	490	450	GAH I	440	440	430
GDV I	470	4 0	420	GGV I	490	510	460	GAV I	470	460	450
HDH I	5 0	490	490	GGV III	480	5?0	490	GAV III	440	440	440
HDV II	470	4 0	420	GGH I	450	450	440				
HDV III	510	500	470	GHH IV	400	390	380				
HEH I	5 0	5 0	5?0	GHV II	490	480	440				
HEH V	440	450	460	GHV III	390	390	380				
HEV I	430	440	430	GHV IV	340	340	330				
HEV II	520	510	510	GJ I	480	480	470				
HEV III	510	510	500	GJ III	420	420	410				
HFH III	470	470	460	GKH I	490	470	470				
HFV I	470	480	490	GKH III	500	500	500				
HFV II	450	440	440	GKV III	510	530	510				
HFV III	450	460	460								
Mean growth	459	456	457		469	468	456		454	451	444

Statist cal nalysis of differences in g owth bet een the consecutive periods above

	—1 → 0	0 → 1	1 → 2	2 → 3	3 → 4	4 → 5
Mean d ff	—3	+1	—2	—12	—3	—7
Stand de	10 70	12 10	11 67	15 37	10 00	13.23
t alue	—1 04–	+0 37–	—0 59–	—3 28××	—1 00–	—1 51–
n al e	20	20	19	19	9	9

Table 23

Reduced oxygen tension with addition of carbon dioxide to prevent hyperventilatory hypocapnia Exposure to 10 per cent oxygen plus 5 per cent carbon dioxide in nitrogen at 1 atm abs for 8 hrs during period 0 with growth recording periods of 24 hrs (—1 0 +1 +2 +3 +4 +5) Longitudinal growth rates in microns in three overlapping series of animals

Animal	—1	0	+1
GBH I	490	470	460
GBH II	480	460	460
GBH V	410	410	410
GCH I	530	510	500
GCH II	480	460	450
GCH III	500	470	450
GCV II	450	430	420
GDH III	390	300	230
HDH II	460	460	400
HDH III	490	460	420
HDH IV	450	440	350
HDV I	480	460	410
HEH II	460	390	370
HEH III	520	510	470
HEH IV	520	510	480
HEV IV	470	440	380
HFH I	490	470	400
HFH IV	540	510	450
HFV IV	450	450	370
Mean growth	*477*	*453*	*415*

Animal	+1	+2	+3
FVH II	420	410	420
FVV I	380	410	430
FVV II	350	370	400
FXH III	5[illegible]0	550	5[illegible]0
FXH IV	530	530	520
FXV I	520	530	520
GGH II	*470*	*490*	*480*
GGH III	480	510	500
GGH IV	520	570	540
GGV II	530	550	540
GHH II	360	390	350
GHH III	400	460	440
GHH V	360	420	380
GHV I	460	500	480
GJ II	430	480	460
GJ IV	410	440	390
GJ V	420	450	450
GKH II	510	550	530
GKV I	500	510	520
GKV II	480	500	540
Mean growth	*454*	*481*	*472*

Animal	+3	+4	+5
FYH I	490	490	460
FYH II	480	480	420
FYH V	460	460	460
FYV I	480	480	460
FYV II	470	470	460
FZH IV	380	370	360
FZV II	*4[illegible]0*	*390*	*400*
GAH III	510	500	490
GAV II	400	400	4[illegible]0
Mean growth	*452*	*449*	*434*

Statistical analysis of differences in growth between consecutive periods above

	—1 → 0	*0 → 1*	*1 → 2*	*2 → 3*	*3 → 4*	*4 → 5*
Mean diff	—24	—38	+27	—9	—3	—14
Stand dev	22 41	28 73	19 49	23 15	5 00	20 68
t value	—4 61×××	—5 83×××	+6 19×××	—1 74−	—2 00−	—2 09−
n value	19	19	20	20	9	9

Ta le 24

Control animals for Table 23 (10 per cent oxygen plus 5 per cent carbon dioxide in nitrogen) Exposed to air for 8 hrs during period 0 Longitudinal growth rates in microns du ing successive periods of 24 hrs (−1 0 +1 +2 +3 +4 +5) in three overlapping series of animals

Animal	−1	0	+1	Animal	+1	+2	+3	Animal	+3	+4	+5
GBH III	450	420	440	FVH III	450	450	450	FYH III	450	450	460
GBH IV	440	440	440	FVV IV	370	350	350	FYH IV	500	490	460
GCH IV	410	470	430	FXH V	540	530	530	FYV III	470	490	470
GCV I	410	410	410	FXV II	550	550	550	FYV IV	490	480	480
GCV III	440	430	450	FXV III	530	520	520	FZH II	440	430	420
GCV IV	480	480	480	FXV IV	550	540	540	FZH III	390	380	390
GDH IV	450	450	440	GGH I	490	490	450	GAH I	440	440	430
GDV I	420	420	420	GGV I	490	510	460	GAV I	470	460	450
HDH I	5 0	490	49	GGV III	480	500	490	GAV III	440	440	440
HDV II	420	4 0	420	GGH I	450	450	440				
HDV III	510	500	470	GHH IV	4 0	390	380				
HEH I	5 0	500	500	GHV II	490	480	440				
HEH V	44	450	460	GHV III	390	390	380				
HEV I	430	440	430	GHV IV	340	340	330				
HEV II	570	510	510	GJ I	490	480	470				
HEV III	51	510	500	GJ III	420	420	410				
HFH III	470	470	460	GKH I	490	470	470				
HFV I	470	480	490	GKH III	500	500	500				
HFV II	450	440	440	GKV III	510	530	510				
HFV III	450	460	460								
Mean growth	459	456	457		469	468	456		454	451	444

Statistical analysis of differences in g owth between the consecutive periods above

	−1 → 0	0 → 1	1 → 2	2 → 3	3 → 4	4 → 5
Mean diff	−3	+1	−2	−12	−3	−7
S and d	10 70	12 10	11 67	15 37	10 00	13 23
t alu	−1 04−	+0 37−	−0 59−	−3 28××	−1 00−	−1 51−
f alu	0	0	19	19	9	9

Table 23

Reduced oxygen tension with addition of carbon dioxide to prevent hyperventilatory hypocapnia Exposure to 10 per cent oxygen plus 5 per cent carbon dioxide in nitrogen at 1 atm abs for 8 hrs during period 0 with growth recording periods of 24 hrs (−1, 0 +1 +2 +3 +4 +5) Longitudinal growth rates in microns in three overlapping series of animals

Animal	−1	0	+1	Animal	+1	+2	+3	Animal	+3	+4	+5
GBH I	490	470	460	FVH II	420	410	420	FYH I	490	490	460
GBH II	480	460	460	FVV I	380	410	430	FYH II	480	480	420
GBH V	410	410	410	FVV II	350	370	400	FYH V	460	460	460
GCH I	530	510	500	FXH III	550	550	550	FYV I	480	480	460
GCH II	480	460	450	FXH IV	530	530	520	FYV II	470	470	460
GCH III	500	470	450	FXV I	520	530	520	FZH IV	380	370	360
GCV II	450	430	420	GGH II	470	490	480	FZV II	[illegible]	390	400
GDH III	390	300	230	GGH III	480	510	500	GAH III	510	500	490
HDH II	460	460	400	GGH IV	520	570	540	GAV II	400	400	[illegible]
HDH III	490	460	420	GGV II	530	550	540				
HDH IV	450	440	350	GHH II	360	390	350				
HDV I	480	460	410	GHH III	400	460	440				
HEH II	460	390	370	GHH V	360	420	380				
HEH III	520	510	470	GHV I	460	500	480				
HEH IV	520	510	480	GJ II	430	480	460				
HEV IV	470	440	380	GJ IV	410	440	390				
HFH I	490	470	400	GJ V	420	450	450				
HFH IV	540	510	450	GKH II	510	550	530				
HFV IV	450	450	370	GKV I	500	510	520				
				GKV II	480	500	540				
Mean growth	477	453	415		454	481	472		452	449	434

Statistical analysis of differences in growth between consecutive periods above

	−1 → 0	0 → 1	1 → 2	2 → 3	3 → 4	4 → 5
Mean diff	−24	−38	+27	−9	−3	−14
Stand dev	22 41	28 73	19 49	23 15	5 00	20 68
t value	−4 61×××	−5 83×××	+6 19×××	−1 74−	−2 00−	−2 09−
n value	19	19	20	20	9	9

CHAPTER 6

RESULTS OF INCREASED CARBON DIOXIDE TENSION IN AIR

The results hitherto presented have shown a variation in growth on alteration of the inspired oxygen tension It has also been demonstrated that the decrease in growth at reduced oxygen is not due to the concommitant reduction of the carbon dioxide tension during the hypoxaemic hyperventilation These observations on hypoxaemia with and without hypocapnia also represent observations on decreased (Chapter 4) and undecreased (Chapter 5) carbon dioxide tension As the effects on growth were not changed by the difference in carbon dioxide tension the conclusion can be drawn that a reduction of carbon dioxide does not influence on the growth as measured here with the limitation of being guilty only in hypoxaemia As mentioned in the introduction venous stasis has been held responsible by various authors for stimulated growth in general and this makes the study of the carbon dioxide factor interesting Does an increased carbon dioxide tension accelerate the growth rate for instance by a vasodilation in bone? To begin with this question can be raised irrespective of the mechanism involved

It was considered advisable to start with a fairly small dose to avoid carbon dioxide toxicity which might be present for instance as a depression on the cartilage cell metabolism The percentages chosen were 3 per cent 5 per cent and 7 per cent Higher doses are not toleratd by human volunteers (Fig 12) Much higher doses can be given to animals before death occurs but it was considered to be of little interest in this investigation to further increase the carbon dioxide tension because of the pronounced effects on the general condition of animals under such circumstances

A Three per cent carbon dioxide in air at 1 atm abs with growth recording periods of 24 hrs

The results are given in Table 25 with control animals in Table 26 The statistical comparison between changes in test and control showed no differences There were no particular changes in the mean values between the seven consecutive days studied

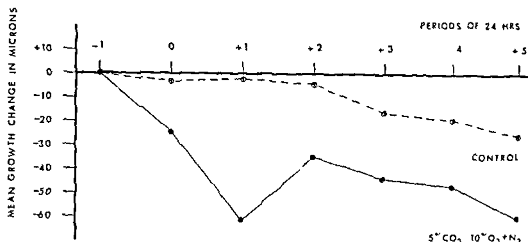


Figure 11

Longitudinal growth of the proximal tibial metaphysis in rabbits at exposure to a gas mixture with 10 % of oxygen and 5 % of carbon dioxide in nitrogen at normal barometric pressure Exposure time 8 hrs during period 0 Growth recordings by oxytetracycline labelling for seven consecutive days Mean growth changes in microns from day to day measured within the same animal Figures made continous by overlapping observations in period +1 and +3

cent oxygen all in nitrogen the rectal temperature of the control animals was in mean 38 6 °C and in the test group 37,9°C The difference was significant which means that the temperature factor had to be taken into consideration later (Chapter 7) Further more this hyperventilation when influencing on the temperature could be expected to influence also on the water balance of the animals To evaluate this possibility 6 animals were exposed as above and the haematocrite and the haemoglobin values of venous blood was determined before and immediately after The haematocrite values ranged between 33 and 44 per cent but without differences between tests and controls The haemoglobin was between 9 6 and 13 6 g per cent also with no difference between tests and controls

It was considered indicated also to study the possible role played by carbon dioxide alone when given in increased dose at an unreduced oxygen partial pressure

Table 26

Control animals for Tables 25 27 and 28 (3 5 7 per cent CO_2) Longitudinal growth rates in microns during successive periods of 24 hrs (−1 0 +1 +2 +3 +4 +5) in three overlapping series of animals

Animal	−1	0	+1	Animal	+1	+2	+3	Animal	+3	+4	+5
BHM I	530	550	570	BQV I	590	590	590	BXV I	540	530	5 0
BPH IV	540	540	540	BQV II	6^0	600	6 0	BXV II	540	540	530
BPH V	560	550	550	BSV I	530	520	500	BVV I	410	4 0	350
BTH III	590	590	600	BSV II	470	440	410	CAH II	450	4 0	350
BTH IV	550	550	550	BUH III	450	450	390	CAH III	370	38	400
BTV IV	530	520	5 0	BUV II	480	480	480	CAH IV	480	480	480
CBH I	560	570	590	BUV III	480	490	480	DCH II	390	390	390
CBV I	470	470	410	BYH II	420	440	420	DCV III	430	410	4^0
CBV III	520	510	50^	BYH III	420	430	470	DDV I	460	460	460
CBV IV	550	540	540	BYV I	410	4 0	4 0	DDV II	460	440	48^
CCV I	570	570	510	BYV II	370	350	340	DEH II	520	520	510
CCV II	520	520	510	BZV I	610	600	590	DEV III	500	500	490
CCV III	520	520	530	BZH II	610	610	6^0	DEV IV	510	510	510
CCH IV	5 0	5 0	5 0	BZV II	55	560	560				
CDV I	5 0	5 0	5 0	DFH III	570	530	510				
CDV II	510	510	490	DFH IV	460	470	460				
CVH III	550	550	510	DFV III	470	470	470				
CVV II	520	510	5	DHH II	550	550	550				
CVV III	550	550	530	DHH IV	540	540	530				
CXH I	500	480	480	DHV II	560	55	530				
CXH II	450	430	410	HQH III	490	490	480				
CYH IV	530	530	510	HQH IV	470	480	490				
CYH V	450	470	470	HRH III	510	5 0	500				
CYV III	510	530	53	HRH IV	52^	540	550				
CYV IV	520	530	530	HRH V	520	520	520				
Mean growth	522	522	513		5 5	504	495		466	457	450

Statistical analysis of differences in growth between consecutive periods above

	−1 → 0	0 → 1	1 → 2	2 → 3	3 → 4	4 → 5
Mean diff	0	−8	−2	−9	−9	−7
Stand de	10 60	17 00	10 68	14.53	15.53	25 94
t value	−0 19−	−2 47×	−0.75−	−3.03××	−.15−	−0 96−
n value	25	25	25	25	13	13

Table 25

Increased carbon dioxide tension at normal oxygen tension by exposure to 3 per cent carbon dioxide in air at 1 atm abs for 8 hrs during period 0 Longitudinal growth rates in microns during successive periods of 24 hrs (—1 0 +1 +2 +3) in two overlapping series of animals

Animal	—1	0	+1	Animal	+1	+2	+3
BPH I	530	530	520	BQH I	610	600	600
BPH II	570	570	560	BQH II	540	540	540
BPH III	560	560	560	BQH III	590	590	590
BPV I	570	570	570	BQH IV	590	580	570
BPV II	570	570	560	BQV III	580	570	570
BPV III	550	550	550	BQV IV	570	570	570
BPV IV	580	570	560	BSH I	460	460	450
BPV V	430	430	430	BSH II	500	500	450
BMH II	550	540	520	BSH III	470	450	470
BMH III	550	530	500	BSH IV	480	450	440
Mean growth	*546*	*542*	*533*		*539*	*531*	*525*

Statistical analysis of differences in growth between consecutive periods above

	—1 → 0	0 → 1	1 → 2	2 → 3
Mean diff	—4	—9	—8	—6
Stand dev	6 99	9 94	10 33	17 76
t value	—1 80⁻	—2 84×	—2 45×	—1 07⁻
n value	10	10	10	10

Table 26

Control animals for Tables 25 27 and 28 (3 5 7 per cent CO) Longitudinal growth rates in microns during successive periods of 24 hrs (—1 0 +1 +2 +3 +4 +5) in three overlapping series of animals

Animal	—1	0	+1
BHM I	530	550	570
BPH IV	540	540	540
BPH V	560	550	550
BTH III	590	590	600
BTH IV	550	550	550
BTV IV	530	520	570
CBH I	560	570	590
CBV I	470	470	410
CBV III	520	510	5[illegible]0
CBV IV	550	540	540
CCV I	520	520	510
CCV II	570	520	510
CCV III	520	520	530
CCH IV	5[illegible]3	500	500
CDV I	500	5[illegible]0	5[illegible]0
CDV II	510	510	490
CVH III	550	55	510
CVV II	520	510	500
CVV III	550	550	530
CXH I	500	480	480
CXH II	450	430	410
CYH IV	530	530	510
CYH V	450	470	470
CYV III	510	530	530
CYV IV	520	530	530
Mean growth	572	522	513

Animal	+1	+2	+3
BQV I	590	590	590
BQV II	600	600	600
BSV I	530	520	500
BSV II	470	440	410
BUH III	450	450	390
BUV II	480	480	480
BUV III	480	480	480
BYH II	470	440	470
BYH III	420	430	420
BYV I	410	4[illegible]0	4[illegible]0
BYV II	370	350	340
BZV I	610	600	590
BZH II	610	610	6[illegible]0
BZV II	550	560	560
DFH III	520	530	510
DFH IV	460	470	460
DFV III	470	470	470
DHH II	550	550	550
DHH IV	540	540	530
DHV II	560	550	530
HQH III	490	490	480
HQH IV	470	480	490
HRH III	510	500	500
HRH IV	55[illegible]	54[illegible]	550
HRH V	520	520	520
Mean growth	505	504	495

Animal	+3	+4	+5
BXV I	540	530	500
BXV II	540	540	530
BVV I	410	4[illegible]0	350
CAH II	450	4[illegible]0	350
CAH III	370	380	400
CAH IV	480	480	480
DCH II	390	390	390
DCV III	430	410	4[illegible]0
DDV I	460	460	460
DDV II	460	440	480
DEH II	520	520	510
DEV III	5[illegible]0	5[illegible]0	490
DEV IV	510	510	510
Mean growth	466	457	450

Statistical analysis of differences in growth between consecutive periods above

	—1 → 0	0 → 1	1 → 2	2 → 3	3 → 4	4 → 5
Mean diff	0	—8	—2	—9	—9	—7
Stand de	10 60	17 00	10 68	14 53	15 53	25 94
t al e	—0 19−	—2 47×	—0 75−	—3 03××	—2 15−	—0 96−
n value	25	25	25	25	11	13

Table 25

Increased carbon dioxide tension at normal oxygen tension by exposure to 3 per cent carbon dioxide in air at 1 atm abs for 8 hrs during period 0 Longitudinal growth rates in microns during successive periods of 24 hrs (—1 0 +1 +2 +3) in two overlapping series of animals

Animal	—1	0	+1	Animal	+1	+2	+3
BPH I	530	530	520	BQH I	610	600	600
BPH II	570	570	560	BQH II	540	540	540
BPH III	560	560	560	BQH III	590	590	590
BPV I	570	570	570	BQH IV	590	580	570
BPV II	570	570	560	BQV III	580	570	570
BPV III	550	550	550	BQV IV	570	570	570
BPV IV	580	570	560	BSH I	460	460	450
BPV V	430	430	430	BSH II	500	500	450
BMH II	550	540	520	BSH III	470	450	470
BMH III	550	530	500	BSH IV	480	450	440
Mean growth	546	542	533		539	531	525

Statistical analysis of differences in growth between consecutive periods above

	—1 → 0	0 → 1	1 → 2	2 → 3
Mean diff	*—4*	*—9*	*—8*	*—6*
Stand dev	6 99	9 94	10 33	17 76
t value	—1 80⁻	—2 84×	—2 45×	—1 07⁻
n value	10	10	10	10

B Five per cent carbon dioxide in air at 1 atm abs with growth recording periods of 24 hrs

The results are given in Table 27 with the control animals in Table 26 The statistical comparison between changes in test and control still demonstrated no significant differences

Table 27

Increased carbon dioxide tension at normal oxygen tension by exposure to 5 per cent carbon dioxide in air at 1 atm abs for 8 hrs during period 0 Longitudinal growth rates in microns during successive periods of 24 hrs (−1 0 +1 +2 +3 +4 +5) in three overlapping series of animals

Animal	−1	0	+1	Animal	+1	+2	+3	Animal	+3	+4	+5
BTH I	570	560	550	BUH I	450	480	470	BXH I	510	500	5 0
BTH II	550	540	540	BUH II	440	440	440	BXH II	550	540	530
BTH V	560	550	530	BUH IV	490	490	450	BXH III	590	580	540
BTV I	560	570	560	BUV I	500	500	480	CAH I	530	530	510
BTV II	590	590	580	BYH I	370	390	350	CAH V	490	490	450
BTH V	510	500	500	BYH IV	400	410	380	CAV II	470	460	480
CBH II	540	550	530	BYV III	360	360	350	CAV IV	490	500	490
CBH III	540	520	530	BZH I	530	520	500				
CBH IV	560	550	520	BZH III	550	540	540				
CBH V	550	550	550	BZV III	570	550	550				
CBV II	530	530	510								
CCH I	500	500	490								
CCH II	520	520	520								
CCH III	500	500	500								
CDH I	400	440	480								
CDH II	5 0	500	500								
Mean growth	530	5 9	524		466	468	451		519	514	500

Statistical analysis of differences in growth between consecutive periods above

	−1 → 0	0 → 1	1 → 2	2 → 3	3 → 4	4 → 5
Mean diff	−1	−5	+2	−17	−4	−14
Stand dev	13 6	15 92	14 76	15 67	7 86	21 49
t value	−0 19−	−1.26−	+0 43−	−3 42××	−1 45−	−1 76−
n value	16	16	10	10	7	7

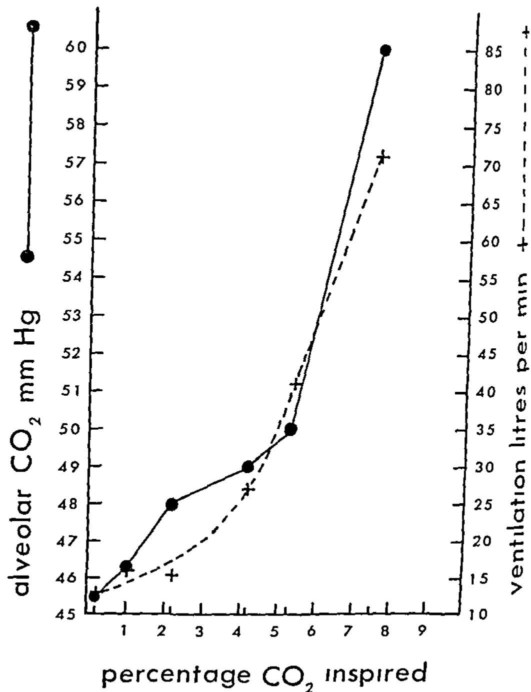


Figure 12

Alveolar CO pressure and ventilation volume at different percentage of CO breathing in man (After Barcroft J Margaria R J Physiol [London] 72 175 1931)

animals simultaneously treated with air alone The controls are added together in one table here as also in Chapter 4 (A—H) for the studies utilizing the hypobaric chamber

As this part of the investigation had not disclosed any changes in growth at a moderate increase in the carbon dioxide tension in air it was considered to be advisable to increase the sensitivity of the test by reducing the observation time to 12 hrs thereby covering ²/₃ of period 0 with the carbon dioxide exposure instead of ¹/₃ as in A—C above Growth measuring periods of 12 hrs were used also in Chapters 3—4 It was decided convenient for the comparisons to keep the same time periods although the toxicity character of carbon dioxide at the doses applied did not necessitate this As no effects had been observed with the carbon dioxide exposures so far 7 per cent carbon dioxide in air was chosen for the 12 hrs study

D Seven per cent carbon dioxide in air at 1 atm abs with growth recording periods of 12 hrs

The results are given in Tables 29 and 30 The statistical comparison between test and control showed no significant influence on the growth rate from this

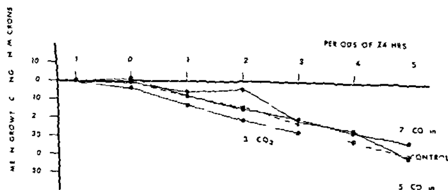


Figure 13

Longitudinal growth of the proximal tibial metaphysis in rabbits at exposure to increased concentrations of carbon dioxide (3 5 7%) in air at 1 atm.abs for 8 hrs during period 0 Growth recordings by oxytetracycline labeling for seven consecutive days Mean growth changes in microns from day to day measured within the same animal Figures made continuous by overlapping observations in period +1 and +3

Table 28

Increased carbon dioxide tension at normal oxygen tension by exposure to 7 per cent carbon dioxide in air at 1 atm abs for 8 hrs during period 0 Longitudinal growth rates in microns during successive periods of 24 hrs (—1 0 +1, +2 +3 +4 +5) in three overlapping series of animals

Animal	—1	0	+1	Animal	+1	+2	+3	Animal	+3	+4	+5
CVH I	550	550	560	DTH II	530	530	510	DCH I	410	370	330
CVH II	550	550	530	DTV II	550	540	540	DCH III	400	400	410
CVH IV	530	520	510	DGH II	560	550	550	DCV II	360	360	380
CVV I	*540*	*540*	*530*	*DGV I*	*550*	*540*	*540*	*DDH I*	*510*	*510*	*510*
CXH III	450	430	410	DGV II	540	570	520	DDV III	490	480	480
CXH V	370	400	400	DHH I	530	530	530	DEH I	500	510	500
CYH I	540	540	540	DHH III	550	550	540	DEH IV	530	530	5[illegible]0
CYH II	510	500	480	DHV I	540	540	520	DEV II	490	480	490
CYV I	5[illegible]0	510	510	DHV III	540	520	500				
CYV II	500	510	490	HQH I	450	450	460				
				HQH II	380	400	430				
				HQV I	480	460	420				
				HQV II	460	460	460				
				HQV III	460	460	440				
				HRH I	490	500	500				
				HRH II	540	530	530				
Mean growth	504	505	496		509	508	501		461	455	450

Statistical analysis of differences in growth between consecutive periods above

	—1 → 0	0 → 1	1 → 2	2 → 3	3 → 4	4 → 5
Mean diff	+1	—9	—1	—8	—6	—5
Stand dev	13 70	11 00	13 10	19 15	15 06	20 70
t value	+0 23⁻	—2 59×	—0 38⁻	—1 57⁻	—1 18⁻	—0 69⁻
n value	10	10	16	16	8	8

C Seven per cent carbon dioxide in air at 1 atm abs with growth recording periods of 24 hrs

The results are given in Table 28 with the control animals in Table 26 The statistical comparison gave the following values —1 → 0 t=0 14⁻ 0 → +1 t=0 10⁻ +1 → +2 t=0 09⁻, +2 → +3 t=0 25⁻ +3 → +4 t=0 43⁻, +4 → +5 t—0 18⁻ The insignificant changes in growth recorded are illustrated in Fig 13 for 3, 5 and 7 per cent carbon dioxide in air and the control

animals simultaneously treated with air alone The controls are added together in one table here as also in Chapter 4 (A—H) for the studies utilizing the hypobari chamber

As this part of the investigation had not disclosed any changes in growth at a mod rat increase in the carbon dioxide tension in air it was considered to be advisable to increase the sensitivity of the test by reducing the observation time to 12 hrs thereby covering ²/₃ of period 0 with the carbon dioxide exposure instead of ¹/₃ as in A—C above Growth measuring periods of 12 hrs were used also in Chapters 3—4 It was decided convenient for the comparisons to keep the same time periods although the toxicity character of carbon dioxide at the dos s applied did not necessitate this As no effects had been observed with the carbon dioxide exposures so far 7 per cent carbon dioxide in air was chosen for the 12 hrs study

D Seven per cent carbon dioxide in air at 1 atm abs with growth recording periods of 12 hrs

The results are given in Tables 29 and 30 The statistical comparison between test and control showed no significant influence on the growth rate from this

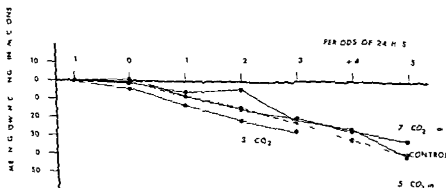


Figure 13

Longitudinal growth of the proximal tibial metaphysis in rabbits at exposure to increased concentrations of carbon dioxide (3 5 7%) in air at 1 atm.abs for 8 hrs during period 0 Growth recordings by oxytetracycline labelling for seven consecutive days Mean growth changes in microns from day to day measured within the same animal Figures made continuous by overlapping observations in period +1 and +3

Table 29

Increased carbon dioxide tension at normal oxygen tension by exposure to 7 per cent carbon dioxide in air at 1 atm abs for 8 hrs during period 0 Longitudinal growth rates in microns during three successive periods of 12 hrs (—½ 0 +½)

Animal	—½	0	+½
ERH II	220	220	200
ERH III	240	230	210
ERV II	250	250	240
ERV III	250	250	240
ESH III	170	160	160
ESH IV	240	230	210
ESV II	250	250	240
ETH I	270	260	260
ETH III	280	270	270
ETV II	270	260	260
HOH I	210	210	210
HOH III	230	240	230
HOH IV	240	230	230
HOH V	230	230	240
HOV I	230	230	230
EPH I	270	270	260
HPH II	250	250	250
Mean growth	241	238	232

Statistical analysis of differences in growth between consecutive periods above

	—½ → 0	0 → +½
Mean diff	—4	—6
Stand dev	6 06	8 70
t value	—2 40×	—2 79×
n avlue	17	17

partial pressure of carbon dioxide in air (—½ → 0 U=0 64⁻, 0 → +½ U= 0 98⁻)

Carbon dioxide at a concentration of 7 per cent in air is a breathing stimulant and this hyperventilation could be expected to lower the body *temperature* (Chapter 6) In 18 animals divided into 9 in test and 9 in control the rectal

Table 30

Control animals for Table 29 (7 % CO in air) Exposed to air for 8 hrs during period 0 Longitudinal growth rates in microns during three successive periods of 12 hrs (−1/2 0 +1/2)

Animal	−1/2	0	+1/2
ERH V	250	240	240
ERV I	190	200	200
ERV IV	250	250	240
FSH I	190	170	180
ESH II	170	170	160
ESV IV	260	250	260
ETH II	240	250	240
ETV I	280	270	260
ETV III	250	290	220
HOH II	230	230	240
HOV II	210	210	210
HOV III	220	220	220
HOV IV	230	220	230
HPH III	240	240	240
HPH IV	240	240	230
Mean growth	230	230	225

Statistical analysis of differences in growth between consecutive periods above

	−1/2 → 0	0 → +1/2
Mean diff	0	−5
Stand dev	13 63	19 59
t value	0	−1 05−
n value	15	15

temperatures were measured immediately at the end of the 8 hrs but no significant difference was observed in this case in contrast to the study of 10 per cent O +5 per cent CO_2 in nitrogen. Therefore no determination was performed on haemoglobin and haematocrite values because the hyperventilation even when inducing a reduced temperature did not alter these values (Chapter 6)

Table 29

Increased carbon dioxide tension at normal oxygen tension by exposure to 7 per cent carbon dioxide in air at 1 atm abs for 8 hrs during period 0 Longitudinal growth rates in microns during three successive periods of 12 hrs (—1/2 0 +1/2)

Animal	—1/2	0	+1/2
ERH II	220	220	200
ERH III	240	230	210
ERV II	250	250	240
ERV III	250	250	240
ESH III	170	160	160
ESH IV	240	230	210
ESV II	250	250	240
ETH I	270	260	260
ETH III	280	270	270
ETV II	270	260	260
HOH I	210	210	210
HOH III	230	240	230
HOH IV	240	230	230
HOH V	230	230	240
HOV I	230	230	230
EPH I	270	270	260
HPH II	250	250	250
Mean growth	241	238	232

Statistical analysis of differences in growth between consecutive periods above

	—1/2 → 0	0 → +1/2
Mean diff	—4	—6
Stand dev	6 06	8 70
t value	—2 40×	—2 79×
n avlue	17	17

partial pressure of carbon dioxide in air (—1/2 → 0 U=0 64⁻ 0 → +1/2 U=0 98⁻)

Carbon dioxide at a concentration of 7 per cent in air is a breathing stimulant and this hyperventilation could be expected to lower the body *temperature* (Chapter 6) In 18 animals divided into 9 in test and 9 in control the rectal

CHAPTER 7

DISCUSSION

The activity of investigation into the bone growth and related problems is considerable A search of the literature through the years 1964—67 by the MEDLARS system of automatic data analysis at the Karolinska Institutet Stockholm Sweden yielded 612 references on *Bone Growth* and 377 on *Blood Flow in Bone and Extremities* The aspect from which the author has investigated this problem concerning endochondral growth of bones seems not to be reported but it has been used in tissue cultures and in studies on wound healing fracture healing and periosteal proliferation (Chapter 1) Changes in the blood circulation arterial as well as venous is closely interrelated to changes in the tensions of the respiratory gases of the tissues besides the concommitant alteration in the transport of other components of the blood It was decided that the growth in length of bones should be analysed at a primary change in the gaseous pressures to see whether a knowledge in this uninvestigated sector of bone physiology would shed some light on the clinical problem of leg length inequality

A sensitive method for recording of growth in length was necessary because the exposures to the test gases had to be short if acclimatization reactions (*Altland & Highman* 1952) and the toxicity of oxygen (*Bean* 1945) were to be avoided (Chapter 2) This means that a daily recording of the growth had to be possible because the oxygen toxicity is induced within hours during pure oxygen breathing at increased barometric pressure both in rabbits and humans (*Binger* et al 1927 *Bean* 1964) The intravital oxytetracycline labelling method was well known at the institution and was the most sensitive for quantitative measurements of daily growth in length in rabbits (*Hansson* 1967) Therefore the choice of this method needs no further discussion

With the aim of inducing alteration first in the oxygen tension and secondly also in the carbon dioxide tension of the blood it seemed convenient to perform this by respiratory gas changes In this way it was possible to utilize data from

This part of the investigation had not demonstrated any effects on the longitudinal growth rates of the proximal tibial metaphysis during or after increase in the respiratory carbon dioxide concentrations to 3—7 per cent fo 8 hrs and with an observation time of 6 consecutive periods of 24 hrs, thus covering the maturing time of the epiphyseal cartilage cells in the growth plate (*Messier & Leblond* 1960) The partial pressure of carbon dioxide in venous blood is in man about 50 mm Hg (*Patterson* et al 1955) which would correspond to about 6 5 per cent CO_2 in air at a pressure of 760 mm Hg The use of 7 per cent here has consequently been well above the normal venous blood tension The partial pressures used in this investigation must have been sufficiently high for the purpose of the study A further elevation of the carbon dioxide tension up to growth depressing concentrations was beyond the scope of this study

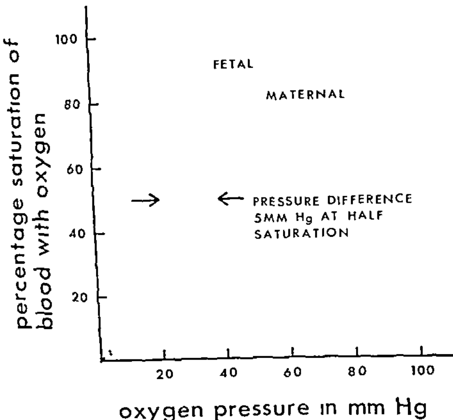


Figure 14

Oxygen dissociation curves of maternal and fetal bloods from rabbits near term (After Barron D H Meschia G Sympos quant Biol 19 93 1954)

and so on These differences are not unknown (*Dittmer & Grebe* 1958) but in this investigation the absolute quantitative changes were of less importance than the principal alterations induced For this reason it was considered to be unnecessary to make special analyses of the blood gas tensions pH and so on in the rabbits used for the study For the ages used in this investigation it can be deduced from the curves of haemoglobin dissociation at birth and at adulthood (Fig 14) that the actual values have been somewhere between the two curves and very near the human dissociation curve (*Dittmer & Grebe* 1958)

The investigation begins with testing of increased oxygen tensions(Chapter 3) with omittance of the intervals earlier tried (*Persson 1967*) It proved to be above the limit of oxygen toxicity to use 100 per cent oxygen for 8 hrs at 2 atm abs as judged by autopsy of the lungs of the animals There was however

the literature of respiratory physiology and at the same time to perform the experiments without direct influences on the extremities, as for instance in perfusion technics This would introduce other factors influencing on growth such as trauma, immobilisation venous stasis or denervation (*Sunden* 1967) It was decided as a comprimise between reduction of errors of the method a avoiding of the oxygen toxicity to use 8 hrs of treatment with increas oxygen tensions, The same times were used for the whole investigation to make comparisons easier, although the toxicity factors of the different exposures wer not the same The treatment was given only once and continuously during th end of the day named period 0 (Fig 2 and 3) This localisation was intended to prevent coverings of eventually disphasic responses (*Persson* 1967)

Experimental works with growing rabbits always result in a considerable mortality during the period when they are no longer feeding from the mo her To reduce errors from this, defined conditions were set out for exclusion of abberant animals in a way which was intended not to influence on the reliability of the results obtained (Chapter 2) By the 6 principles for exclusio the total number of animals in this investigation was reduced from 1079 to 948 which seems reasonable in rabbits of this age (Table 1) Of this material 737 rabbits were controls with notes on age, weight and longitudinal growth of th proximal tibial metaphysis all measured on the same day With the rabbits arranged in groups of 5 days difference in age there was found to be a significan or highly significant positive correlation between the weight and the growth in length (Chapter 2) This is not in accordance with *Hansson* (1967) but his analysis was performed within each litter and with animals excluded below defined weight limits

The statistical treatment of the material is described in Chapter 2 It was decided that comparisons of changes in growth should be based on changes within each animal thereby reducing the variation in the samples regarding their growth in absolute values Only three consecutive time periods of growth were measured in each animal and to cover the total maturing time of the cartilage cells (*Kember* 1960 *Messier & Leblond* 1960) three overlapping series of animals were used in each study thereby giving a series of 7 consecutive days of growth (Fig 2 and 3) The mean differences of growth from day to day within the same animal are illustrated in the figures Some figures are in addition made up as vertical comparisons of the growth in absolute mean values between a test group and a control group both made up of litter mates

Some basic principles and data from the respiratory physiology are mentioned in the end of chapter 2, concerning mostly alveolar and blood gas tensions at the partial pressures of gases used in this investigation Many of these values are from human experiments but as the rabbit has about the same oxygen dissociation curve (Fig 14) of haemoglobin and the same pH the same principles apply to them, although the absolute values can be a bit different because of differences in body temperature temperature regulation respiratory dead space

s much During period —1 the growth differs only 7 microns in mean value urin° period 0 it differs 22 microns and during period +1 it differs 23 microns -etween test and control The same difference in absolute growth rates between est and control remains during period +1 to +3 (Tables 6 and 7) but in the ast series of animals covering periods +3 to +5 there seems to be no diffe -ence in the mean values This could be a coincidence but it implies that the timulation had ended after about 72 hrs that is during period +3 about This is illustrated in Fig 7 The type of calculation used for Fig 7 has not been used for the statistics because it introduces another error which was considered to be principally larger i e comparison of changes in growth rates which are not within the same animal Unless the samples are very large it can not be expected that the mean growth in the control group should be the same as in the test group as measured in absolute values of growth It is probable that the stimulation recorded in period 0 measured to about 3 per cent above the control is so near the error of the method (*Hansson* 1967 *Persson* 1967) that it was impossible to get a significant measure of the return to a normal growth rate if this return occurs over a couple of days around period +3 thus measuring only some per cent from one day to the other It should also be noted that at the age of rabbits used there is a normal decrease in growth rates of about 1 per cent daily (Fig 15) Variations in this could influence on occasional samples

To conclude on the analysis of increased oxygen tensions there was found to be a small stimulation of the longitudinal growth of the tibial proximal metaphysis during breathing of 100 per cent of oxygen at 1 atm abs for 8 hrs In the series with 24 hrs as the labelling period the increase was 3 per cent When the labelling period was 12 hrs instead the increase should have been about 6 per cent theoretically as will be explained below It was noted to be 5 per cent (Chapter 3) This means that the actual increase in growth during the oxygen treatment in period 0 (that is 8 hrs of the 12 or 24 hrs used as the labelling interval) should have been about 7 5 to 9 per cent above the growth rate before treatment This conclusion can be made because of the positioning of treatment in relation to the oxytetracycline injections (Fig 2—3) in such a way that period 0 ends very close to the end of the oxygen treatment. This makes the hrs before the start of treatment still included in period 0 to have a growth rate like that of the control day named period —1 as long as there is no *diurnal variation* (*Persson* 1968) *It is not possible* to say if the increase in growth rate mentioned was the same during all the 8 hrs of hyperoxygenation It is of interest to compare this degree of stimulation with the values reported after peripheral nerve division (*Sunden* 1967) also in rabbits and with the oxytetracycline method In comparison between the operated and the non operated side there was a difference of 23 *per cent on* the sixth day after the nerve section with the higher growth rate on the paralyzed side. This seems to be a greater stimulation but it should be remembered that there might have

a small but statistically insignificant increase in growth during the oxygen treatment at 2 atm abs followed by a significant decrease in growth during the 12 hrs after withdrawal of oxygen This might be the result of the oxygen toxicity to the lungs (*Smith* 1899) as it was not observed when the oxygen pressure was reduced to 100 per cent at 1 atm abs At this tension there was no mortality and no lung changes either and the increase in growth during the treatment was now statistically significant measuring 5 per cent in absolute mean value compared to the controls The results mentioned above were achieved with growth recording periods of 12 hrs The decrease in growth during the time period immediately after the hyperoxygenation observed at 2 atm abs was not significant after a continous exposure for 8 hrs at 1 atm abs of pure oxygen When the observation time was extended for 5 days after the gas exposure (Chapter 3, C) the same changes were observed with a significant increase in growth (+3 per cent compared to the control) during the period of hyperoxygenation but with no further changes with comparison between test and control for the following 5 days This should imply that the stimulation of growth which was observed to start during the hyperoxygenation continued for the following time periods If it had ceased suddenly there should have been a decrease in growth again with comparison between the changes in test and control from some period to the next, and this was not the case Only during period +5 in the test group there was a significant decrease in growth but in comparison with the changes in the control group this significance was lost There was also a significant decrease in growth during period +1 compared to period 0 but this is of the same magnitude both in test and control The reason for this decrease in both groups might be that the animals had been taken away from their mother for the first time during the day before and also that intravenous injections had been started the day before that Such stress factors could have some temporary influence on the growth rate There is also another possible factor in this decrease From the earlier investigations of hyperoxygenation at 1 and 2 atm abs but with growth recording periods of 12 hrs reported above there had been significant signs of such a decrease When the measuring microscopy is performed as a blind test it is possible that expectancies of changes influence on the readings within the limits of error of the labelling line identification But the blind handling in this case will affect the control and test equally thereby eliminating some significances when the comparison is performed between the changes in test and in the control Returning to the observations made at 1 atm abs during 100 per cent of oxygen breathing for 8 hrs and with growth recording periods of 24 hrs the question remains to be answered if the stimulation during the exposure proceeds also on the following days which is suggested by the fact that no later decrease is statistically verified Looking at the absolute values of growth rates (Tables 6 and 7) it seems as if the increase in growth during period 0 in the test group is lost during periods +1 but in the control group the values of growth decrease

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been a certain retardation also on the control side, due to the catabolic phase after the operation This factor has been shown to influence on the growth rate measured with the same technic by *Hansson* (1967) He recorded a relative stimulation of growth after medullary plugging of tibia measuring up to 10 per cent above the control side This is more of the magnitude measured in the present study It is not possible with the available information, to say whether the calculated growth acceleration (+7 5 to 9 per cent) observed during hyperoxygenation was near or far from the maximal growth rate of the cartilage that is if oxygen, at least for a short time, can speed up the growth rate fully, or if other factors are of greater importance in addition

The effects on growth seen during oxygen breathing may theoretically be due to some secondary factor and not to the changes in oxygen availability itself However breathing 100 per cent of oxygen does not seem to influence on arterial pH and pCO (*Dittmer & Grebe* 1958) although smaller changes occasionally are reported Heart rate blood pressure and vascular resistance are also nearly unchanged (*Egger* et al 1962) Ventilation volumes have been reported to be slightly decreased (*Hejneman* 1943) but also to be increased (*Lambertsen* et al 1953) It has been advocated to be an accumulation of carbon dioxide in tissues during hyperbaric oxygenation, due to blocking of the haemoglobin by the oxygen (*Bean* 1945) *Lambertsen* et al (1953) have shown that this is not the case in rabbit breathing 3 5 atmospheres of pure oxygen This was investigated by analysis of subcutaneous carbon dioxide gas depots and there was no increase above the controls until after 4 hrs of oxygen treatment that is when the pulmonary toxicity influences on the gas exchanges Thus there is no unequivocal support for the possibility that the growth effects of oxygen is mediated by the abovementioned factors Changes in the respiratory oxygen tensions influence also on the blood circulation which will be discussed below in connection with decreased oxygen tensions and changes in the carbon dioxide tension which are also vasoactive

Results of **decreased oxygen tensions** are given in Chapter 4 This part of the investigation comprises 461 accepted animals distributed on hypoxic conditions corresponding to air breathing at 3000 4000 5000 and 6000 meters altitude in a hypobaric chamber and on exposures to 12 and 10 per cent of oxygen in nitrogen at normobaric environmental pressure The experiments showed that 3000 meters (corresponding to a pO of about 108 mm Hg) did not statistically affect the growth rates of the proximal tibial metaphysis for the time of exposure used At 4000 meters there was a highly significant decrease in growth from the day of exposure to the day after and another highly significant increase in growth from the first day after to the second day after exposure (Chapter 4 F) The arithmetic mean of the decrease was 11 per cent and of the following increase it was 5 per cent in comparison between changes in the test and in

the control group The result at 5000 meters were about the same At 6000 meters the effects were still more pronounced now with a highly significant decrease in growth on the day of treatment compared to the day before measuring 9 per cent in mean difference This was followed by a further decrease of 70 per cent to the day after treatment, still highly significant From period +1 to period +2 after treatment there was again a significant increa e in growth, now measuring a little more than 4 per cent only

These results were obtained in a hypobaric chamber To rule out the pos ibility that the effects on growth were caused by other factors than the reduction in the oxygen pressure the analysis was continued by testing 12 per cent and 10 per cent of oxygen in nitrogen at a normal barometric pressure The s me tendencies were again observed with a decrease in growth from the day before to the day of treatment measuring 7 per cent at 10 per cent of oxygen From the day of treatment to the day after there was another signi ficant decrease of 7 per cent In this connection it should be remembered that the relation between exposure and measuring periods was the same as in the pure oxygen studies This means that the reduction of 7 per cent recorded during the hypoxic exposure implied that the actual reduction were three times greater that is about 21 per cent during the 8 hrs of treatment within the 24 hrs of oxygen labelling in period 0 If the same considerations are applied to the studies on simulated altitudes we can deduce that the decrease in growth during hypoxic conditions (4000—6000 meters) were between 10 5 per cent and 33 per cent The growth rate during the day after treatment was in general a little less depressed than these figures contrary to the impression given by the illustrations (Fig 8 and 9) Returning to the study of 10 per cent of oxygen in nitrogen there was no statistical significance in the increase of growth from period +1 to +2 contrary to the altitude exposures Looking at the absolute values however there was such an increase which was significant in the 10 per cent oxygen test group and not significant in the corresponding control group With comparison between the two groups this s gnifi ance was lost The mean difference between periods +1 and +2 was +6 per cent which is the same magnitude as earlier observed in the hypobaric chamber The samples used at the 10 per cent of oxygen test were however fairly small at these time periods (10 and 9 animals in test and control) It was therefore concluded on the basis of the total material that the effects on the long tudinal growth were the same wether the hypoxia was caused by means of a hypobaric chamber or by exposing the animals to a gas mixture with oxygen of the corresponding partial pressure For the utilized time of exposure it can further be con luded that 3000 meters does not influence on growth that is a barometric pressure of about 520 mm Hg and an oxygen partial pressure of about 110 mm Hg compared to the normal pressure 159 mm Hg At 4000 and 5000 meters there were pronounced but temporary effects on growth At 6 00 meters or a 10 per cent of oxygen (pO about 75 mm Hg) the reduction was more pronoun

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For a further understanding of the possible effects caused by carbon dioxide on growth it was studied during normoxic conditions also Addition of carbon dioxide to air could influence on growth rate by influence on the oxygen tensions due to hyperventilatory increase of the alveolar ventilation or to Bohr-effects on the haemo lobin disociation curve as discussed above for the hypoxaemia experiments It could also influence on the bone blood flow (see later) Growth recordings were made at 3 5 and 7 per cent of carbon dioxide in air at 1 atm. abs. for 8 hrs No significant effetcs on the growth rates were observed (Chapter 6) Observations were made for five days after the end of the exposures An increased growth could have been expected by the fact that the hyper

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In Chapter 5 results are presented from testing of **ten per cent of oxygen in combination with five per cent of carbon dioxide in nitrogen**. A comparison of the changes in growth from day to day between test and control showed, that there was a decrease in growth between the day before and the day of exposure measuring 4 per cent in mean, a further decrease of 8 per cent during the 24 hrs after exposure (+1) and finally an increase during the next day (+2) measuring 8 per cent. All these differences between the test group and the control group were highly significant. This means that the effects on growth in length of the metaphysis were about the same in the hypoxic experiments whether the carbon dioxide tension was allowed to be reduced by the hyperventilation or not. This in turn means that the change in growth was induced by the changes in oxygen tension.

At this point it is of interest to discuss the differences between hypocapnic and normocapnic hypoxia which differ with regard to the haemoglobin dissociation curves leading to differences in the amount of oxygen available

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At this point it is of interest to discuss the differences between hypocapnic and normocapnic hypoxia, which differ with regard to the haemoglobin dissociation curves leading to differences in the amount of oxygen available

at a given oxygen tension *Lennox and Gibbs* (1932) have determined the the oxygen and carbon dioxide contents of arterial and venous femoral blood in humans inhaling various mixtures containing these gases and nitrogen. At an oxygen concentration of 6—12 per cent in nitrogen the arterial oxygen content decreased from 17.5 to 16.5 vol. per cent and the venous oxygen content from 13.5 to 12.3 vol. per cent. At the same time the arterial carbon dioxide content decreased from 51.4 to 49.5 vol. per cent and the venous carbon dioxide content changed from 54.1 to 54.3 vol. per cent as a mean of 4 test subjects. When 4—6 per cent of carbon dioxide was added to the same oxygen concentration the arterial oxygen content decreased from 18.8 to 16.5 vol. per cent, the venous oxygen content from 15.6 to 13.3 vol. per cent and the carbon dioxide content increased in arterial blood from 47.7 to 49.1 vol. per cent and in venous blood from 50.2 to 51.0 vol. per cent. The changes recorded means changes from normal air breathing to the test gas specified after 10—15 min. The referred values imply that the addition of carbon dioxide was enough to counteract the reduction in carbon dioxide tension caused by hypoxic hyperventilation at an oxygen concentration of 8—12 per cent in nitrogen. About the same inspiratory gas concentrations were used in the present investigation. It also means that the addition of carbon dioxide did not reduce the magnitude of decrease in the arterial oxygen content during 8—12 per cent of oxygen breathing. This could have been suspected for the reason that the added *carbon dioxide further increases the hyperventilation caused by the* hypoxia. On the other hand it could also have been expected to be a reduced oxygen content in the blood after the addition of carbon dioxide due to the increased acidity and the resulting 'Bohreffect' on the haemoglobin dissociation curve which gives a reduction in the oxygen binding capacity at increased carbon dioxide tensions (*Steen* 1968). The reported oxygen contents above (*Lennox & Gibbs* 1932) showed this tendency. It is possible that these two counteracting effects (hyperventilation and Bohr effect) of the added carbon dioxide explain why no difference was demonstrated in the growth rate studies. Effects on the blood flow could also be expected from the added carbon dioxide (see later).

For a *further understanding of the possible effects caused* by carbon dioxide on growth it was studied during normoxic conditions also. **Addition of carbon** dioxide to air could influence on growth rate by influence on the oxygen tensions due to hyperventilatory increase of the alveolar ventilation *or to Bohr effects* on the haemoglobin disociation curve as discussed above for the hypoxaemia experiments. It could also influence on the bone blood flow (see later). Growth recordings were made at 3, 5 and 7 per cent of carbon dioxide *in air at 1 atm.* abs. for 8 hrs. No significant effetcs on the growth rates were observed (Chapter 6). Observations *were made for five days after the end of the exposures.* An increased growth could have been expected by the fact that the *hyper*

ventilation that is induced increases the alveolar oxygen tension Furthermore an increased oxygen availability in the bone could have been caused by the Bohr effect In contrast to its consequences during hypoxic conditions, it has theoretically a promoting effect on the oxygen transport during normoxia This is due to the fact that the dissociation curves at normocapnia and at hypercapnia coincide at a normal arterial oxygen tension but divide at a reduced oxygen tension liberating more oxygen in the capillary system The gain in oxygen availability caused by this mechanism is probably too small to give measurable effects on growth, and the same is probably the case with the gain due to hyperventilation The moderate increase in growth caused by a five folded oxygen tension (Chapter 3) makes this conclusion reasonable On the other hand it could have been a slight depressing effect on the cell metabolism from the increased carbon dioxide tension counteracting the increased oxygen availability Finally, it is also possible that carbon dioxide influences on the bone blood flow (see later)

In addition to the discussion of the separate results above, some common factors will be considered below, that is the possible effects caused by changes in temperature and in the bone blood flow

As mentioned **temperature** has been considered to be a possible regulant of growth rate in bones although no unequivocal results have been presented as to the possibilities of using it as a stimulant of growth (Chapter 1) Rabbits are known to regulate temperature by breathing and this fact introduces the possibility that effects on growth at changes in the gaseous environment are concommitant with alterations in the body temperature To evaluate this possibility rectal temperatures were recorded in some of the series Exposure to 100 per cent of oxygen at 1 atm abs did not influence on the temperatures (Chapter 3) In this case the conclusion is that the increase in growth simultaneously recorded was not due to change in temperature It was expected to be a maximal hyperventilation at exposure to a combination of decreased oxygen and increased carbon dioxide tensions This test was therefore chosen for the next determination of temperatures that is the exposure to 10 per cent of oxygen and 5 per cent of carbon dioxide in nitrogen (Chapter 5) There was found to be a significant decrease in body temperature at the end of the exposure measuring in mean 0 7°C In this case there were concommitant decreases in temperature and in growth To see whether this decrease was due to the hypoxia or to the increased carbon dioxide tension in the inspired gas temperature recordings were also performed at the same oxygen tension but without addition of carbon dioxide It was performed on 7 animals after 8 hrs at 5900 meters corresponding to an oxygen concentration of 10 per cent at 1 atm abs No changes were observed compared to the temperatures before exposure and to 5 control animals Addition of 7 per cent carbon dioxide to

air for 8 hrs did not change the temperature either (Chapter 6) The conclusion is that the changes in growth were not concommitant with changes in the rectal temperature except in one experiment which does not warrant any conclusion as to the possibility that the growth can be altered by local change in temperature Determination of haemoglobin content and haematocrit value (Chapter 5) did not show any change during the exposure indicating that the decrease in temperature was coincident with any significant loss of fluid

The next special factor is the **influences on the blood flow** from the alteration in gas tensions studied It is well documented that both oxygen and carbon dioxide may be vasoactive altering the blood flow with changes in tension This has been studied regarding the femoral blood flow (*Lennox & Gibbs* 1932) Increased oxygen tensions gave slightly reduced flow rates (*Bird & Telfer* 1966) decreased oxygen tensions gave considerable increases (*Boon & Marotta* 1964) and finally increased carbon dioxide tensions gave slight increases in sympathectomized limbs but slight decreases in normal limbs (*Steck & Gellhorn* 1939) There are however no reports on the changes in the intraosseous blood flow under the circumstances mentioned Therefore this was specially studied using the heat clearance method described by *Sunden* (1967) and the gas tensions used in the present investigation There turned out to be no consistent effects measurable on the blood flow in the epiphysis These experiments will be separately published (*Persson & Sunden* 1968) The indication at present is that the effects on growth described in this investigation were achieved without measurable changes in the bone blood flow

The next part of the discussion will be devoted to the **time lags between the exposures and the recorded effects on growth** with the intention of evaluating which cells of the cartilage plate that have highest sensitivity to the treatments This problem is presented in Chapter 4 where determinations of the height of the cartilage plate are reported For the following discussion a summarizing figure (Fig 16) is given concerning some principal growth effects obtained with increased and decreased oxygen tensions and increased carbon dioxide tensions The figure depicts the growth ratios between test and control for each day with litter mates in both groups It is made up from the absolute values of growth in microns The overlapping samples in the time periods +1 and +3 have been summarized. From this figure (Fig 16) it is clear that the effects on growth were recorded already during the exposure to the artificial gas mixtures rich or poor in oxygen This means that the effect was elicited in the zone of degenerating cells where the tetracycline was built in labelling the growth process The curves give the impression that the hypoxic depression

ventilation that is induced increases the alveolar oxygen tension Furthermore an increased oxygen availability in the bone could have been caused by the Bohr effect In contrast to its consequences during hypoxic conditions it has theoretically a promoting effect on the oxygen transport during normoxia This is due to the fact that the dissociation curves at normocapnia and at hypercapnia coincide at a normal arterial oxygen tension but divide at a reduced oxygen tension liberating more oxygen *in the capillary system The gain in oxygen* availability caused by this mechanism is probably too small to give measurable effects on growth, and the same is probably the case with the gain due to hyperventilation The moderate increase in growth caused by a five folded oxygen tension (Chapter 3) makes this conclusion reasonable On the other hand *it could have been a slight depressing effect on the cell metabolism from* the increased carbon dioxide tension, counteracting the increased oxygen availability Finally, it is also possible that carbon dioxide influences on the bone blood flow (see later)

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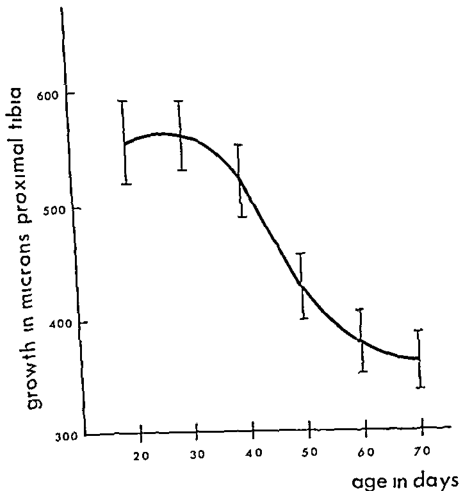


Figure 15

Growth rate from the proximal growth plate of the tibia of rabbits according to Hansson (1967)

bility due to circulatory disturbances (*Ackerman & Brinkley* 1966) as for instance in pathological fracture healing (*Coulson* et al 1966 *Goulon* et al 1968) Regarding the introductory question of venous stasis or arterial hyper aemia as the possible mechanism behind unilateral stimulation of bone growth this investigation does not positively support the assumption that venous stasis should stimulate the growth Arterial hyperaemia seems more in line with the

(10 per cent O +N) is greater during the day after exposure than during th exposure This is due to the fact earlier mentioned that the day of exposure includes about 16 hrs of normal growth before the 8 hrs of treatment and decrease in growth This means that the actual growth rate under the hypoxic condition was somewhat three times greater than recorded in the figure In other words the decrease in growth rate is about the same during the hypoxic exposure as during the following 24 hrs (period +1) If the same reasoning is applied to the pure oxygen breathing it would imply that the growth in period 0, recorded in Fig 16 as a stimulation of 4 per cent in reality comprised 16 hrs of normal growth rate and 8 hrs of about 12 per cent increase in growth This means that the stimulation is greater during the oxygen exposure than during the following days The conclusion must be that th hyperoxygenation accelerated the growth during the treatment and that this acceleration slowly subsided during 1—4 days after In conclusion it may be suggested that *degeneration and calcification of the cartilage cells is an oxygen depending process* easily disturbed by changes in the oxygen tension of blood This could also be expected by the fact that this is the zone where the cartilage cells meet the blood vessels of the metaphysis (*Trueta & Amato* 1960)

The question can now be raised whether the changes in metaphyseal growth rate represent only alterations in the position of the calcifying frontier of a temporary duration or if they represent true changes in the growth in length of the bone In other words are the effects limited to the degenerating zone or are they affecting a more extended series of cells in different stages of maturation? This problem was studied by determinations of the height of the cartilage plate in combination with the growth recordings (Chapter 4) After exposure to decreased oxygen partial pressure there was an almost significant decrease in the height of the plate indicating effects also on cartilage cells at other maturing stages than those undergoing degeneration Measurment of the cartilage plate has not yet been made at increased oxygen tensions although it seems interesting to know, whether the recorded growth acceleration represents a temporary advancement of the calcifying frontier with a decrease in the height of the plate or if it is combined with an unchanged or increased height of the cartilage plate signifying that the stimulation also affected the younger cells of the cartilage

The demonstrated sensitivity to changes in the oxygen tension and the lack of sensitivity to changes in the carbon dioxide tension does not mean that it should be possible to increase the height of a person by increasing the environ mental oxygen tension The oxygen toxicity especially to the lungs would very soon eliminate the stimulation, and might even result in a total decrease in growth On the other hand the demonstrated importance of the oxygen tension might have some application in conditions of decreased oxygen availa

CHAPTER 8

SUMMARY

Leg length inequality in children is sometimes caused by one sided growth stimulation after fractures osteomyelites or arterio-venous fistulae This knowledge has resulted in experimental and clinical attempts to induce such a stimulation in a short leg This literature is shortly reviewed with special reference to the suggested causative factors particularly arterial hyperaemia venous stasis local temperature and the local oxygenation

For studying the oxygen factor in this respect and secondly also the carbon dioxide factor young rabbits were exposed to changes in the partial pressures of the respiratory gases utilizing pressure chambers and artifical gas mixtures The exposures were for 8 hrs and given only once Defined principles were set up for exclusion of abnormal animals The longitudinal growth of the proximal tibial metaphysis was recorded by intravital oxytetracycline labelling and ultra violet microscopy performed as a blind test.

It was found that oxygen tensions above 100 per cent at 2 atm abs was above the tolerance due to the pulmonary oxygen toxicity At 100 per cent of oxygen at 1 atm abs there was a stimulation of growth during the exposure subsiding for about 1—4 days When the oxygen tension was reduced below normal there was a decrease in growth during the exposure and during the following 24 hrs of about the same magnitude but thereafter the growth approached the normal The oxygen tension limits of these effects were determined The height of the cartilage plate seemed to be reduced one day after the hypoxia implying effects on an extended series of maturing stages of the cartilage cells For elimination of the hyperventilatory hypocapnia under the hypoxic condition carbon dioxide was added to the low oxygen mixture without changing the growth effects. Addition of carbon dioxide to air did not influence on the growth within the doses tested Rectal temperatures were checked without showing co-variation in more than one case

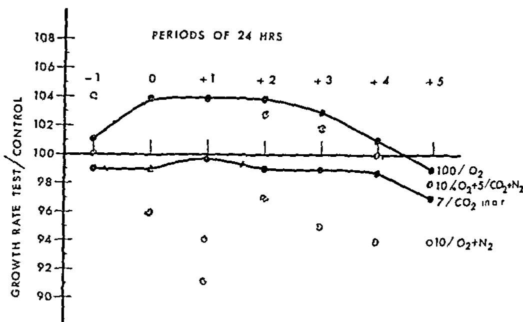


Figure 16

Daily growth in length of the proximal tibial metaphysis in rabbits measured by oxytetracycline labelling given as growth rates of tests in per cent of growth in control groups Respiratory gas altered for 8 hrs during period 0 Gas compositions given in figure Ambient pressure 1 atm abs

findings but on the other hand it can not be assumed that venous stasis is always concommitant with a decrease in the local blood flow It is theoretically possible that a venous stasis with an increased venous pressure can be compensated by a local arteriolar dilatation keeping the pressure difference and the blood flow on a normal level Attempts to measure the bone flow during venous stasis are so diverging in the results that this might be the case (*Herzig & Root* 1959 *McPherson* et al 1961 *Valderrama & Trueta* 1965 *White & Stein* 1965) If venous stasis stimulates growth it must not anyhow be combined with any significant reduction of the local oxygen tension unless it comprises other factors compensating for the hypoxic growth retardation

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Bjorn Mauritz Persson

It was concluded from the immediate effects on growth at changes in the oxygen tension, that the cartilage cells in the zone of degeneration and calcification were very sensitive implying an oxygen depending nature of this process The lack of sensitivity to changes in the carbon dioxide tension was discussed with reference to venous stasis and arterial hyperaemia as mechanisms behind over-growth of a long bone

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SVEN ARNE AHI GREN

RATE OF APPOSITION OF DENTINE IN UPPER INCISORS IN NORMAL AND HORMONE TREATED RATS

WITH A TENTATIVE COMPARISON OF THE APPOSITION OF DENTINE AND LAMELLAR BONE



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ACTA ORTHOPAEDICA SCANDINAVICA
SUPPLEMENTUM NO 116

From the Department of Orthopaedic Surgery (Head Prof G Wiberg) and the Department of Oral Roentgenology (Head Prof K Å Omnell) University of Lund Sweden

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BY

SVEN ARNE AHLGREN

MUNKSGAARD
Copenhagen 1968

Statistical adviser Peter Vorwerk
Translator L J Brown

LUND 1968
CARL BLOMS BOKTRYCKERI A B

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EXPLANATIONS

Throughout the investigation apposition of dentine is measured in arbitrary units — measuring units (1 unit = 10 μm).

The various technical terms used such as section, interval, point, etc. are explained on pages 35—36 and 52. The abbreviations used in Tables in the Appendix are explained on pages 46—47.

Tables with Roman numbers are collected in the Appendix.

INTRODUCTION AND PURPOSE OF THE INVESTIGATION

In the course of personal preliminary experimental investigations on the effect of the growth hormone on the rate of bone repair and lamellar bone formation it was realised that accurate quantitative determinations would offer considerable technical difficulties Because of the constant remodelling of bone tissue the interpretation of the results could be difficult

Bone repair has been studied by manual testing of the stability of the fractured bone (Koskinen 1959 1965) by roentgenography with or without planimetric measurement of the callus as seen in the roentgenogram (Koskinen 1959 1963 1965) by examination of histologic sections (Koskinen 1959 1965 Hulth & Olerud 1964 Pritchard 1964) by autoradiography (Koskinen 1959 1965) by measurement of the mechanical strength of the fractured bone during healing (Lindsay & Howes 1931 McKeown Lindsay Harvey & Howes 1932 Falkenberg 1961 Wray & Goldstein 1966) by studying the uptake and disappearance of radioactive isotopes (Marshak & Byron Jr 1945 Bauer 1954 Bohr 1955 Wendeberg 1961) by angiography (Gothman 1961 Hulth & Olerud 1964) by tetracycline labelling (Hulth & Olerud 1964) and by microradiography (Nilsonne 1959 Hulth & Olerud 1964)

Lamellar as well as cancellous bone has been widely studied also with the aid of radioactive isotopes (Bauer Carlsson & Lindquist 1961 Dymling 1964 Nordin Smith & Glass 1964 Bauer 1966) microradiography (Jowsey 1966) and vital dyes such as alizarine (Harris 1960) and the tetracyclines (Harris 1960 Lee 1963 1964 Frost Villanueva & Roth 1960 Tapp 1966)

During the above mentioned personal investigations interest was focused on dentine This tissue is similar to bone but its physiology is

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ceedin, to the investigation of dentine is a test tissue for hormonal influence it was considered necessary to re investigate the normal rate of apposition of incisor dentine in the rat Several experimental investigations of the action of the growth hormone have been performed on female rats It was therefore primarily decided to confine the investigation to rats of this sex The study was limited to the upper incisors for two reasons First owing to their shape it is easier to obtain acceptable histologic sections from these teeth than from the lower incisors and second to keep the number of histologic sections and measurements within reasonable limits

Since it was desired to compare dentine and bone formation it was decided to study endosteal and periosteal bone formation because bones in the rat have no Haversian systems (Enlow & Brown 1958)

The purposes of the present investigation were

to chart the normal pattern of apposition of dentine of the upper incisors in the female white rat

to find out whether the rate of apposition of dentine could be influenced by the administration of a hormone and

to compare the rate of apposition of dentine and of lamellar bone

less complicated because no resorption occurs in normal dentine It was *thought that its rate of formation could be studied* with comparatively simple laboratory methods It had been realised by the Swedish anatomist Retzius as early as 1838 that "similarity between dentine and bone is closer than that suggested by the first microscopic examinations *Also other investigators have* recognised such similarities (Weidenreich 1925 Orban 1957 Ørvig 1958 1967 Bernick & Ershoff 1964 Zussman & Joachim 1964)

According to Sognnaes (1955) the microstructural organisation of bone *enamel* dentine and cementum is comparable insofar as they all contain (a) a fibrous framework (b) an amorphous ground substance and (c) inorganic crystals deposited in that order whereas the vascular and cellular elements of bone cementum dentine and enamel decrease in significance in that sequence

Bone and dentine resemble one another also in chemical composition and ultrastructure In both tissues the bulk of the organic matrix consists of collagen and the collagen in dentine is very similar to that in bone (Piez & Likins 1960 Eastoe 1964 1967) The mineral phase in both tissues is an apatite (De Jong 1926 Gross 1926 Hodge 1955 Carlstrom & Engstrom 1956 Posner 1960)

Bone and dentine differ from one another in one essential respect in bone formation and resorption occur simultaneously in normal dentine only formation (Schour 1938 Schour & Massler 1943 b Sognnaes 1955) but as in bone exchange of ions takes place (Armstrong 1955 Sognnaes 1955)

In the incisors of rodents dentine continues to form throughout the animal s life In his studies on the parathyroid glands and calcium metabolism Erdheim (1911) considered the incisors of the rat to be an extremely sensitive indicator He also stressed what may be called their kymographic properties what was registered remained until the incisor was worn away He compared the incisor with bone where the continuous formation and resorption make the interpretation of a microscopic section very difficult and recommended the use of the incisor in investigations of calcium metabolism *Also in fairly recent literature* incisor dentine formation in the rat has been described as continuous very regular and very sensitive to experimental interference (Schour & Massler 1962)

Preliminary personal investigations *showed that* the rate of apposition of dentine in the upper incisors of the white rat varied in a more complicated way than previously supposed Therefore before pro

EARLIER INVESTIGATIONS

MORPHOLOGY OF THE UPPER INCISORS, PARTICULARLY OF THE DENTINE AND A SHORT NOTE ON BONE FORMATION

INCISOR

Gross morphology

According to Mummery (1924) "the distinguishing features of the rodent dentition are the presence in each jaw of a pair of long curved incisors with chisel shaped edges and growing from persistent pulps" (Figs 1—2)

Eruption of the incisors and formation of dentine occur simultaneously and continuously throughout the animal's life This growth is normally counterbalanced by mechanical attrition at the incisal edges (Weinreb Assif & Michaeli 1967)

The upper incisor has been described as a 210° segment of a logarithmic spiral with a lateral shear (Schour & Massler 1962) but also is a segment of a circle about 210° at 5 months of age (Addison & Appleton 1915) The length of the upper incisor along the outer convex side at 5 months of age (Addison & Appleton 1915) is 23 3 mm the extra alveolar length 8 7 mm

The main part of the rat incisor consists of dentine The labial aspect and part of the lateral and medial aspects are covered with a layer of enamel the rest with a thin layer of cement (Figs 2—3)

The longitudinal or "extrusive" growth of the incisor can be measured either as eruption rate or as attrition rate (Sessle 1966 Weinreb et al 1967) Sessle found these values to be close to each other in the lower incisors In the upper incisors the situation is similar Thus according to Addison & Appleton (1915) the rate of attrition is 2 2 mm/week Similar figures have been given by Schour & Massler (1962) and Stuben & Knothe (1965) for the rate of eruption

I

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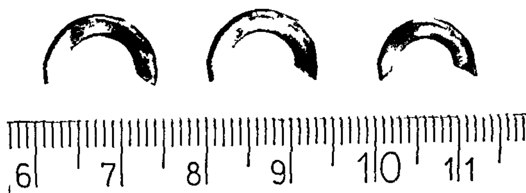


Fig. 1 Incisors from rats of different ages Ages (left to right) approx 10 4 and 2 months Incisal edge to left

Fig 2 Photomicrograph of a section of an incisor (After Erdheim 1911) Symbols P—pulp S=enamel D=dentine SE=enamel epithelium O=odontoblasts AP alveolar periosteum A=the bony alveolus of the tooth M=oral mucous membrane N=incisal end of the tooth The other symbols used are not essential to the understanding in this connection

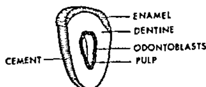


Fig. 3 Schematic drawing of transverse section of an incisor

Dentine

Dentine is formed by odontoblasts lining the pulp cavity (Figs 2—3) and giving off cell processes extending through the dentine tubules. Owing to the continuous eruption of the tooth the odontoblasts move towards the incisal edge at the same time as dentine formation continues (Schour & Massler 1962). During this process the layer of dentine grows thicker and the pulp space consequently narrower.

The first stage in dentine formation consists of the formation of an organic matrix which later becomes calcified (Erdheim 1911, Schour & Massler 1962, Bevelander & Nakahara 1966, Symons 1967). As in the osteone the mineralisation does not follow immediately after the formation of the matrix but a zone of uncalcified tissue, the predentine, normally exists like the osteoid (Frost & Villanueva 1960 a).

Besides collagen, the main organic constituent (Stack 1955, Battistone & Burnett 1956, Piez & Likins 1960, Lastoe 1964, 1967) and small amounts of other proteins, the matrix contains mucopolysaccharides, lipids, citrate and lactate (Stack 1955, Lastoe 1967).

The mineral of dentine — like that of other mammalian hard tissues — consists mainly of an apatite. In normal dentine there is probably only one crystalline phase with a structure resembling that of hydroxyapatite (Carlstrom 1955, Jenkins 1966, Trautz 1955, 1967).

Earlier studies on the rate of apposition of rat incisor dentine

In 1921 Marshall stated: "The interstitial growth of the dentine of the persistent teeth of the rat, as shown by azo dyes under the microscope, amounts approximately to 0.01 mm per day."

Schour and co-workers have performed several studies on the rate of dentine apposition using sodium fluoride or alizarine red S as intravital markers or calculating the rate during known time periods of experimental interferences. They claim the daily rate of apposition of dentine in the white rat's incisors, from 40 days of age onwards, to be very close to 16 μm (Schour & Smith 1934, 1935, Schour & Steadman

1935 Schour 1936 Schour & Hoffman 1935 1937 1939 a and b Schour & Massler 1962) During the early life of the animals the rate is somewhat higher (Herzberg & Schour 1941)

Weinmann (1942) measured the rate of apposition of dentine in the upper incisors of the white rat after injection of alizarine red S and strontium chloride The values given for the daily appositional rate deviated only moderately from the 16 um given by Schour and co workers except one value where the rate is given as 9 5 µm Differences in the rate after injections of alizarine red S and strontium chloride were found and were attributed to a difference in toxicity of the two substances the former substance being the more toxic one

In an extensive survey of dentinogenesis Symons (1967) refers to Schour and co workers and states In the rodent incisor the 16 um increments represents the amount of dentine laid down and calcified daily '

BONE

The periosteal and endosteal formation of new bone in the shafts of long bones occurs by appositional growth on existing surfaces and is a comparatively simple process Concentric layers of new bone form and the process can be compared to the formation of annual rings in a tree (Frost Roth Villanueva & Stanisavljevic 1961 Sissons 1961 Vanderhoeft Kelly & Peterson 1962)

II

INTRAVITAL MARKERS IN THE STUDY OF RATE OF APPOSITIONAL GROWTH OF DENTINE AND BONE

Vital dyes and radioactive isotopes have been widely used as markers in calcified tissue research. John Belchier (1736), who found that the bones of pigs fed madder root stained red, also noticed that the teeth were stained.

Administration of an appropriate marker at suitable intervals results in the development of bands visible microscopically in histologic sections. If the time intervals are known and the distances between the bands measured, the rate of formation of tissue can be expressed as a linear measure per unit of time.

For a marker to be acceptable for the present investigation it should produce bands not only in growing dentine but also simultaneously in growing lamellar bone. Perusal of the literature in the search for a suitable marker revealed that in the rat the appositional growth of dentine had been studied with the aid of different markers. Marshall (1921) tried several vital dyes including alizarine. Pfluger (1931) used uroporfyrin. Alizarine red S (Schour & Hoffman 1939 b, Weinmann 1942, Johannessen 1961), strontium chloride (Weinmann 1942), *sodium* fluoride (Schour & Hoffman 1939 b) and chlorazol fast pink B (Johannessen 1961) have also been used.

Several of the dyes used by Marshall (1921) did not stain satisfactorily. The staining properties of alizarine were satisfactory, but the use of this dye affected the weight gain of the animals. Also Weinmann (1942) found that alizarine had toxic effects. Studying bone formation Harris (1960) and Harris, Travis, Friberg & Radin (1964) observed a toxic effect of alizarine red S. Of the other markers mentioned, sodium fluoride and strontium chloride are known to interfere with mineralisation (Schour & Smith 193?, Weinmann 1942, Pindborg

1935; Schour 1936; Schour & Hoffman 1935, 1937, 1939 a and b; Schour & Massler 1962). During the early life of the animals the rate is somewhat higher (Herzberg & Schour 1941).

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1950 Yaeger Hinrichsen & Cohen 1964 Yaeger 1966) and chlorazol fast pink B with the weight gain of the animals (Johannessen 1964) Uroporfyrin seemed to be less readily available

It was soon realised that it was among the tetracyclines that the marking agent was to be sought The staining properties of the tetracyclines were *initially observed simultaneously in the skeleton and in the teeth* (André 1956 Rall Loo Lane & Kelly 1957 Milch Rall & Tobie 1957 1958) where they are deposited in the enamel and dentine undergoing calcification at the time of administration of the marker and form a compound with yellowish fluorescence in UV light (Zipkin & Larson 1960 Bevelander Rolle & Cohlan 1961 Bayne & Miller 1961 Owen 1961 Owen Stevenson & Keilin 1962 Hulth & Olerud 1962 Harcourt 1963 *Storey 1963 Yaeger Hinrichsen & Cohen 1964 Bevelander 1964* Bennett & Law 1965 Bevelander & Nakahara 1965 Lofgren Nylen & Omnell 1965 Zistava Malek Zak & Kole 1966 Zussman 1966 Bennett 1967)

They accumulate also in bone where mineralisation is active (Ghosez 1959 Harris Jackson & Jowsey 1962 Urist & Ibsen 1963) and form a compound fluorescing in UV light

They are bound to the mineral and possibly also to the matrix (Steendijk 1964 Bevelander & Nakahara 1965) It has been suggested that calcium salt reacts more readily in the initial stage of formation of apatite than later (Urist & Ibsen 1963)

The potential value of the tetracyclines in studies of the rate of dentine *formation has been realised but not exploited* by Gron & Johannessen (1961) and Hulth & Olerud (1962)

In skeletal tissues the tetracyclines have been used in studies of bone grafts (Puranen 1966) lamellar bone formation (Harris 1960 Vanderhoeft Kelly & Peterson 1962 Frost 1960 1962 Frost Roth Villanueva & Stanisavljevic 1961 Frost & Villanueva 1960 Frost Villanueva & Roth 1960 Frost Villanueva Roth & Stanisavljevic 1961 Hulth & Olerud 1962 Stanisavljevic Roth Villanueva & Frost *1962 Holmes* 1963 Lee 1963 1964 Landeros & Frost 1964 Landry & Fleisch 1964 Tapp 1966) endochondral calcification and bone formation (Hulth & Olerud 1962 Hansson 1964 1967 Tapp 1966 Sunden 1967) and callus formation (Milch et al 1958 Urist & Ibsen 1963 Hulth & Olerud 1961)

Tetracyclines may have certain side effects such as *discoloration of the teeth in children and enamel hypoplasia* (Schwachman & Schuster 1956 Schwachman Fekete Kulczycki & Foley 1958 Wallman & Hilton *1962 Hamp 1967*) inhibition of calcification in enamel and dentine in

the rat incisor (Bevelander et al 1961) retardation in development of the skeletal system in the chick embryo (Bevelander Nakahara & Rolle 1960) disturbed mineralisation in tissue cultures of embryonic mice bone (Saxen 1965 1966) retardation of skeletal growth in the dog (Owen 1963) and disturbed endochondral bone growth in the rabbit (Hansson 1967)

The disturbances of tooth development vary with the type of tetracycline used and the dose given and probably also with the route of administration For children Wallman & Hilton (1962) believed oxytetracycline to be less toxic than tetracycline This opinion is shared by Kienitz (1964) Studying the effect on enamel of rat incisors Omnell Lofgren & Nylen (1966) and Löfgren Omnell & Nylen (1968) found oxytetracycline to produce less severe disturbances than tetracycline hydrochloride

In the incisors of the rat Antalovska & Kralova (1966) found a hypomineralised band in the dentine after having fed the animals a diet containing tetracycline hydrochloride The daily dose was about 13 mg/kg bodyweight Gron & Johannessen (1961) found that a dose of oxytetracycline of 10 mg/kg bodyweight did not produce any microradiographically demonstrable hypomineralisation in dentine in the molars of the white rat In dogs even considerably larger doses (Owen 1963) had no effect on the degree of mineralisation of the dentine investigated with microradiography

Even if the degree of mineralisation may be affected it does not necessarily follow that also the rate of matrix formation will be impaired Information on this point is rather scanty A search of available literature failed to reveal a comparative study of the rate of appositional growth of bone or teeth measured by tetracycline marking and by some other method Neither could any study be traced of the rate of such appositional growth after different doses of tetracycline

Cohlan Bevelander & Tiamsic (1963) found the growth in length of the fibula in premature infants to be *decreased during the administration of tetracycline Chu O Hara & Keitel (1964)* could not find any disturbances of the growth process in the fibula but they used oxytetracycline and in smaller doses The mode of administration was also different *Owen (1963)* gave large doses of tetracycline chlortetracycline and oxytetracycline daily to *young dogs for 4* weeks He found retardation of bodyweight *increase* and longitudinal growth of radius and femur only after the administration *of chlortetracycline* This retardation ceased on withdrawal of the agent and was followed by

rapid growth Hansson (1967) considered oxytetracycline to be the least toxic of the tetracyclines and used it in his study of endochondral bone growth Oxytetracycline was also used by Sunden (1967) in a similar investigation These investigators used rabbits as experimental animals and gave 1 mg oxytetracycline/kg bodyweight In an investigation of the growth in length of the tibia in young rats Tapp (1966) used tetracycline in a dose of 75 mg/kg bodyweight He compared the results obtained with the tetracycline method with those obtained with a radiological method and found a disparity The tetracycline method was considered more accurate The possibility of a toxic effect of tetracycline was not discussed

When the tetracyclines have been used as markers in lamellar bone fairly large doses have been given In a survey Tetracycline bone labeling Frost et al (1961) say *About 75 milligrams per kilo in animals is adequate* The dosage of chlortetracycline to dogs employed by Lee (1964) varied between 20 and 50 mg/kg bodyweight intravenously Tapp (1966) gave 75 mg tetracycline/kg bodyweight to rats

In a survey of The effect of tetracycline on mineralization and growth" Bevelander (1964) concludes "absence of adverse side effects when trace amounts are administered *However he did not state what* could be considered as traces

Summarising, the use of oxytetracycline in small doses carries at most a small risk of interfering with mineralisation and/or appositional growth of dentine and lamellar bone It was therefore decided to use this marker in the present investigation

BRIEF SURVEY OF EFFECTS OF PITUITARY GROWTH HORMONE OR HYDROCORTISONE ON DENTINE AND BONE

INTRODUCTION

In the investigation of the possibility to influence the rate of apposition of dentine it was decided to use 2 agents, one expected to accelerate dentine formation and one expected to retard it. The growth hormone and hydrocortisone were selected (see below).

The following survey of the effects of the hormones is extended to comprise the effects observed in dental and skeletal tissues not only in some experimental animals but, for comparison, also in man.

PITUITARY GROWTH HORMONE

Pituitary growth hormone (GH) is a protein and has been extracted from the hypophysis of various animals. Extensive surveys of the chemistry and physiology of growth hormone have been given by Knobil & Hotchkiss (1964), Matsuzaki & Raben (1965) and Evans, Briggs & Dixon (1966). A species specificity exists: in man only GH from man and monkeys is said to have any effect, while the rat responds to GH from several species (Papkoff & Li 1962, Raben 1962 a).

It is an anabolic agent and promotes the growth of most tissues. In man and experimental animals GH has been found to promote nitrogen retention (Bartlett 1955, Russell 1955, Shorr, Carter, Smith Jr, Kennedy, Hazel, Roberts, Sonkin & Livingstone 1955, Beck, McGarry, Dyrenfurth & Venning 1958, Bergenstal & Lipsett 1960, Henneman, Forbes, Moldawer, Dempsey & Carrol 1960). In mineral metabolism retention of calcium, phosphorus, sodium and potassium has been reported (Shorr et al. 1955, Beck et al. 1958, Raben 1962 a). However also the opposite effect on the calcium balance has been observed

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(Knobil & Hotchkiss 1964) GH also influences fat and carbohydrate metabolism (Campbell 1955, Greenbaum 1955 Shorr et al 1955 Henneman & Henneman 1960 Raben 1962 a)

In hypopituitarism in man dental development is retarded while in acromegaly and gigantism the excessive production of the growth hormone can lead to overgrowth of the mandible supra eruption of teeth and increased size of dental arch (Schour & Massler 1943 a Garn Lewis & *Blizzard 1965, Jenkins 1966)*

The effects of GH on rat incisors seem to have received comparatively little attention Schour & van Dyke (1932 a) and Schour (1934 a) found severe changes in the incisors of the hypophysectomised white rat The eruption was poor the teeth were distorted and abnormally small After the administration of the *growth promoting hormone of the pituitary* the eruption rate of the incisor increased but the histological alterations were not significantly influenced (Schour & van Dyke 1932 b Schour 1934 b) Baume Becks Ray & Evans (1954) found hypophysectomy to cause a rapid decrease in the eruption rate of the upper incisors in the rat Dentinogenesis was affected but less severely than amelogenesis They also described folding of the incisors and diminished pulp space findings which have also been made by other investigators (Becks Collins Simpson & Evans 1946 Christensen & Pindborg 1950)

In normal animals the administration of growth promoting hormone did not alter the eruption rate but increased bodyweight (Schour & van Dyke 1932 b Schour 1934 b) Becks Collins Asling Simpson Li & Evans (1948) treated normal female rats for several months with growth hormone They found increased activity of the odonto and ameloblasts in the incisors No change of eruption rate was found Baume Becks & Evans (1954) found administration of growth hormone *to normal adult female rats to have no effect on the rate of incisor* eruption but the teeth increased in size *None of the above mentioned* investigators carried out any studies on the rate of apposition of dentine

Asling & Evans (1961) have surveyed the regulation of skeletal development by the anterior pituitary Their account is based chiefly on data from the rat Pituitary dwarfism and short stature in man have been successfully treated with GH (Raben 1962 b Tanner & Whitehouse 1967) The effect of GH on skeletal tissue in human acromegaly is well known Growth hormone normalises skeletal development in hypophysectomised rats and causes overgrowth in normal rats (Evans Becks Asling Simpson & Li 1948 Asling Simpson Moon Li & Evans *1955 Asling Simpson & Evans 1965)* The tibia test is a bioassay for

GH which increases the epiphyseal width in hypophysectomised female rats (Evans Simpson Marx & Kibrick 1943 Greenspan Li Simpson & Evans 1949 Geschwind & Li 1955)

Koskinen (1959 1963) claimed GH to accelerate fracture healing in man and in the rat

HYDROCORTISONE

Cortisone and hydrocortisone (cortisol) are glucocorticoids and have a catabolic effect (Ashmore & Morgan 1967) The effects they produce on systemic administration are similar (Asboe Hansen 1958)

In the rat Schour & Rogoff (1936) found the calcification of dentine to be disturbed after adrenalectomy

Goldsmith & Ross (1953) gave cortisone to pregnant rats and found "accelerated differentiation and organization" of the odontoblastic layer in the lower incisors of the offspring They also discovered signs of increased deposition of dentine Administration of cortisone retards dentinogenesis in the molars of white rats (Johannessen 1964)

In children with Cushing s syndrome (Liddle 1967) and after the administration of corticosteroids (Friedman & Strang 1966) growth is decreased The osteoporosis occurring in Cushing s syndrome and after therapeutic administration of the hormones is known (Isaksson & Lindholm 1965 Klein Villanueva & Frost 1965 Collins 1966) The healing of fractures is said to be retarded in patients with Cushing s syndrome (Asboe Hansen 1958)

Similar findings have been made in experimental animals after the administration of glucocorticoids *vi* retarded growth in young rats (Sissons & Hadfield 1955 Storey 1960 Ailabouni Dikstein Zor & Sulman 1966) retarded formation of lamellar bone in the rat (Stanisavljevic Roth Villanueva & Frost 1962) and impaired bone repair in the rat (Duthie & Baker 1955 Koskinen 1959 Storey 1960 Hulth & Olerud 1964) and the rabbit (Ragan Howes Plotz Meyer Blunt & Lattes 1950 Gothman 1961)

AUTHOR'S INVESTIGATION

MATERIAL AND METHODS

ANIMALS

Sprague Dawley rats were used. It was initially intended to breed all the animals at the experimental unit in order to know their ages with a high degree of accuracy. However, it was discovered that the weights of such animals at 10 months of age were lower than expected from the normal weight curve for animals from a breeding centre. From then on adult animals were purchased from a breeding centre. When young animals were required, pregnant rats were bought and their young were used when they had reached desired age.

After arrival the animals were observed for at least a week before being used in the experiments. The same room was used for all experimental categories. Cycling of light and darkness was achieved by artificial light. The mean temperature ranged from about 24°C as measured during 5 days in February to about 26°C as measured during 5 days in July. The relative humidity was slightly below 40 per cent. Only minor variation of the temperature and humidity was found during an uninterrupted 48 hour control period. The animals were kept in the same type of cages and fed the same diet (pellets and water *ad libitum*) as in the breeding centre. The pregnant and lactating animals were given a special type of food. During the experiments the animals were weighed at regular intervals.

Of the 271 animals used in the experiments proper, only one died.

VITAL MARKING

Oxytetracycline (OTC) was used (Terramycin® Pfizer). The stock solution contained 50 mg OTC per ml and was diluted in physiologic saline before use.

injections were given on days No 0 8 12 20 and 24 These intervals were chosen because it was initially thought advisable to use periods that were multiples of each other Preliminary experiments had also shown that when the experimental period was about 3—4 weeks the pattern of growth of the dentine during this period could be traced in about half of the number of histologic sections to be taken from the tooth (In some experiments [page 76] OTC was given at 6 day intervals)

Young animals received 0 5 mg (vol 0 5 ml) and adult animals 2 mg (vol 1 ml) OTC at each injection This means that the dose given to normal animals never exceeded 10 mg OTC/kg bodyweight In each experimental category the OTC was injected at the same time of day

Four days after the last injection of OTC the animals were sacrificed (on day 28) by ether The upper incisors and femur and tibia on both sides were removed either immediately or after storage of the cadavers in the deep freeze The bones were afterwards placed or replaced in the deep freeze for later investigation The choice of a 4 day interval between the last injection of OTC and sacrifice was based on the assumption that apposition of dentine during this interval could be measured and included in the investigation and on the fact that measurement to the innermost fluorescent band was easier when it was not situated too close to the dentine border

HISTOLOGIC TECHNIQUE

After fixation in 70 per cent ethyl alcohol for at least 24 hours the teeth were embedded in Ward s Bioplastic

In preliminary experiments both longitudinal and transverse *sections* were prepared However as a rule longitudinal sections permitted only measurement of distances between fluorescent bands *in the middle* part of the tooth The fluorescent bands in the apical and incisal ends were not always well defined which *made it impossible* to measure the distances between them with acceptable precision This haziness of the bands was thought to be due to technical difficulties in the preparation of the sections which were in turn at least partly ascribable to the spiral shape of the tooth Nor did they allow examination around the whole periphery of the tooth Transverse sections proved easier to prepare and to be more informative

The plastic blocks were ground until the contours of the tooth viewed from the side were clearly *visible* through a thin layer of the embedding material The planes in which the transverse sections were to be



Fig. 4. Part of transverse section showing 4 fluorescent bands. The 3 located close to each other produced by intraperitoneal injections of OTC and the single more central one by an intravenous injection. The drawing shows position of photographed part in the transverse section. About 10 mg OTC/kg bodyweight. Adult female rat. 86×

Before deciding upon the route of administration the fluorescent bands produced by intraperitoneal and intravenous (into a tail vein) injections were compared in respect of clearness. Five adult female rats were given 3 consecutive intraperitoneal injections of OTC (about 10 mg/kg bodyweight) at intervals of approximately 24 hours. Eight days after the last of these injections the animals were etherised, the femoral vein was surgically exposed and the same dose of OTC was injected into it. No appreciable difference was found between the clearness of the first 3 fluorescent bands and that of the fourth (Fig. 4). Being technically simpler the intraperitoneal route was therefore chosen for the administration of OTC.

Oxytetracycline was given at intervals of 8, 4, 8 and 4 days, i.e. the

of radiation was an Osram super pressure mercury lamp HBO 200 W. The primary filters were BG 38/2.5 and BG 12/4, allowing transmittance of light with a wavelength between 3300 and 5000 Å. As a secondary filter a barrier filter 50 (Schott) was used. An ocular (Kpl 12.5 ×) was equipped with a 10 mm micrometer divided into 100 parts. The objective was planachromatic 10 × (NA 0.22) magnifica

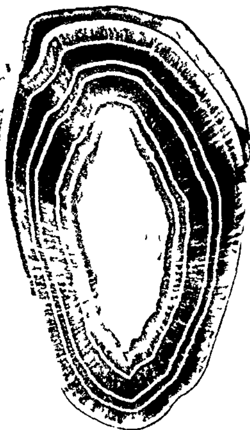


Fig. 6

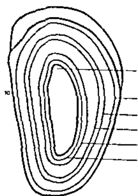


Fig. 7

Fig. 6. Photomicrograph of a transverse section from an incisor. The fluorescent bands can be seen. The radial striations reflect dentine tubules. 3 ×

Fig. 7. Schematic drawing of a transverse section showing location and numbers of the measuring points and the fluorescent bands.

placed were determined in the following way the mid point of an imaginary line connecting the apex and the incisal edge was determined and a line was drawn at right angle to it The 2 right angles thus formed were divided into 2 equal parts Each of these 4 parts was then likewise divided into 2 equal parts These radial lines were marked on the block (Fig 5 a) The marking was facilitated by the use of a glass plate with engraved lines

Segments of the tooth (Fig 5 b) were cut with a circular saw and ground manually to a thickness of approximately 70—100 µm The grinding technique was essentially that described by Frost (1958) for bone Each section was placed dry on slide and covered with a cover glass

MEASURING TECHNIQUE

A conventional binocular microscope (Zeiss Oberkochen) equipped *with an accessory for fluorescence microscopy was used The source*

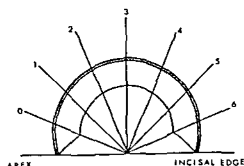


Fig 5 a

Figs 5 a and 5 b Schematic drawing showing location and number of histologic sections Fig 5 a shows lines for intended segmentation of tooth Fig 5 b segments cut with the saw These are later ground to histologic sections of suitable thickness

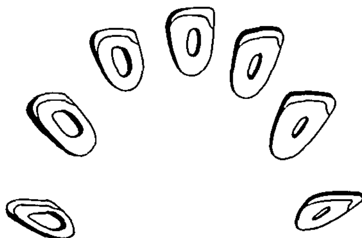


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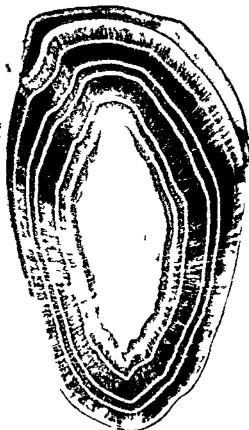


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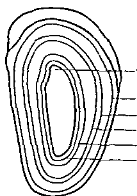


Fig. 7

Fig. 6. Photomicrograph of a transverse section from an incisor. Five fluorescent bands can be seen. The radial striations reflect dentine tubules. 37 ×

Fig. 7. Schematic drawing of a transverse section showing location and numbers of the measuring points and the fluorescent bands.

tion The calibration was made so that each part (unit) in the ocular micrometer corresponded to 10 µm

Distances between consecutive fluorescent bands as measured in the direction of the dentinal tubules (Fig 6) were determined at points numbered 1—10 (Fig 7) The bands were numbered 1 to 5 (Fig 7)

Measuring was started at point 1 and continued around the section Measuring points 1 2 3 and 7 were fairly easy to identify Points 4 5 6 and 8 9 10 were distributed evenly along the lateral and medial aspects At point 2 the thickness of the entire dentine layer, from the dento enamel junction to the pulp (=DL pulp distance=height of the dentine layer), was measured

The fluorescent bands were usually well defined Attempts were always made to measure the distance between the peripheral borders of consecutive fluorescent bands this part of the bands forming first As a rule the positioning of the eyepiece was not difficult except in some areas where the tubules were slightly curved and an approximation had to be made (Fig 6) In the sections situated nearest the mesial edge bands 4 and 5 were sometimes very close to each other At points 1 and 3 they could sometimes not be distinguished from one another and then the distance between them was said to be 0 The distances found between bands at various points were entered in separate record sheets one for each section

PRELIMINARY ANALYSIS OF THE MEASURING METHOD

It soon became obvious that the technical measuring difficulties varied with the location of the section It was also more difficult to measure the distance between a fluorescent band and the pulp outline than between 2 fluorescent bands

To test the precision of the measuring technique a number of sections from animals used only for preliminary investigation were measured by the author and by a specially trained assistant Distances between 2 consecutive fluorescent bands and between a band and the outline of the pulp chamber were measured The sections used allowed measurement at every point from 1 to 10 Each distance was measured twice The author performed 3520 and the technical assistant 3920 measurements

Owing to the construction of the measuring device over or under measurement of the distance by one major grade (5 measuring units) occasionally occurred Therefore as a precaution when a difference

of at least 4 units was found between double determinations a third measurement was made and then those 2 of 3 measurements that appeared most correct were used

Analysis showed that the distance between a fluorescent band and the pulp chamber was more difficult to measure This was exemplified by the residual standard deviation which was approximately 50 per cent higher in spite of the above mentioned procedure with a third measurement This distance was therefore not used separately in the subsequent investigations

Concerning the distance between 2 consecutive fluorescent bands on the basis of 38 sections measured by the author and 39 sections measured by the technical assistant it was found that the reproducibility of double determinations in sections 1—4 was similar and for these taken together For the author it was 0 56 ± 0 18 and for the technical assistant 0 69 ± 0 17 The corresponding figures for section 5 were 0 73 ± 0 10 and 0 72 ± 0 21 respectively Tabulation and a rough comparison showed that the measurements could be made with approximately the same precision at all points No significant difference was found between the absolute values noted by the 2 examiners

In the actual experiments measurements were made by the technical assistant and by the author and each distance was measured on 2 days The measurements made by the assistant were controlled by the author in randomly selected sections

PREPARATION FOR STATISTICAL ANALYSIS

The continuous eruption of the incisors prevented the occurrence of 5 fluorescent bands in all sections 0 to 6 A loss of material occurred because of *missing bands*" *Some injections of OTC* resulted in the appearance of only faint bands or no bands at all Finally some sections were torn or damaged during preparation Thus the vast material available was not complete in every respect but had to be surveyed and arranged to provide maximal information To facilitate the understanding of what follows it might be convenient here to give a list of certain definitions

S e c t i o n designates each of the transverse regularly spaced histological sections of the incisor and are numbered 0 to 6 inclusive according to their distance from the apex (Figs 5 a and b)

B a n d A fluorescent band resulting from administration of OTC The band produced by the last administration of OTC is given the

tion The calibration was made so that each part (unit) in the ocular *micrometer corresponded to 10 μm*

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in each of 3 sections from the middle of the tooth towards the incisal edge

As to the young rats the distances between bands 3—4 and 4—5 were investigated in sections 3 to 6 inclusive and from 2 to 6 respectively Only in sections 5 and 6 were all 4 distances regularly represented in these young animals

Hereinafter these sets will be referred to as 3—4 4—5 3 4 5 and 6 with above mentioned meanings for adult and young animals These sets were used whether the statistical calculations were made on the basis of observations at all 10 measuring points taken together or at a single measuring point In this system section 0 is of no use Section 6 is useful only when investigating young animals It was studied in a few adult animals but at this level apposition of dentine seemed to have stopped almost completely and measurement of distances between the inner bands was very difficult or impossible When section 5 was located too far incisally the same difficulties were encountered

When double determinations of the distances had been made the material was surveyed and divided into the above mentioned sets right and left side separately Then the 2 observations in each set were compared If the difference between the 2 determinations was 4 (measuring) units or more the distance was measured a third time and those 2 that appeared to be most correct were used In an experimental series 5 sets were made for the right tooth and 5 for the left in adult animals and 4 in young animals When the analysis was made on the basis of all 10 measuring points taken together 50 measured values (100 with the second determination) were necessary when set 4—5 was to be investigated it was 40 (80) for the other sets from right and left tooth in each animal If one or more values for a given tooth was missing the tooth could not be included in this analysis When the individual measuring points were investigated the demands were not so high and consequently more material could be used

STATISTICAL METHODS

Owing to the large number of data to be handled the statistical analysis was made with a computer This required the transfer of the values to punched cards In one of the computer programs selected only one value could be registered on each card In each card entries were made not only of the value measured but also of the total height of the dentine layer at point 2 and an identification code com

number 5 and is situated nearest the pulp, the one produced by the first injection being situated nearest the periphery and is given the number 1. The bands in between are numbered 2, 3 and 4 (Fig. 7).

I n t e r v a l refers to time. Interval 1 is the period between the 2 first injections of OTC, i.e. those injections resulting in bands 1 and 2. *Interval 2 is the period between the second and third injections of* OTC resulting in fluorescent bands 2 and 3. Accordingly, interval 3 is the period between the third and fourth injections of OTC (bands 3 and 4) and interval 4 the period between the fourth and fifth injections of OTC (bands 4 and 5).

D i s t a n c e s are to be understood as the distances along the dentinal tubules between fluorescent bands at different points. These distances are the linear measures of the amount of dentine formed during a given period. This measure is given in measuring units (1 unit = *10 µm) throughout the investigation and called measured value, value measured or observation.*

M e a s u r i n g p o i n t s are the places on the periphery of the tooth (Fig. 7) which were selected for measurement of distances between fluorescent bands along the dentine tubules.

S e t. To obtain a picture of the pattern of dentine apposition from different points of view the observations were arranged in certain combinations and such a combination is called a set.

The purpose of the arrangement of observations into sets was to find out whether and if so how the rate of apposition of dentine varied within a certain period between the sections and — in a single section — how the rate of apposition varied during different intervals.

The distances between bands 1—2 and 2—3 were regularly found only in sections 3, 4 and 5. It was thought that this number of sections was not large enough to allow satisfactory statistical analysis. The following sets were found suitable.

The distances between bands 3 and 4 were found to occur rather regularly from section 2 to 5 inclusive. It seemed suitable to study apposition during this 8 day interval through 4 sections.

The distances between bands 4 and 5 (a 4 day interval) were, as a rule, represented in sections 1 to 5 inclusive and provided a set.

The distances between all the 5 bands were rather regularly found in sections 3, 4 and 5 and each of these constituted a set.

Thus the rate of apposition of dentine during an 8 day and a 4 day interval could be investigated in different sections. The rate during different intervals of the entire experimental period could be studied

the possible influence of OTC on the rate of dentine apposition the following experiments were made Twenty five young animals were divided into 3 groups of 8 8 and 9 animals and given intraperitoneal injections of OTC 1 0 10 0 and 20 0 mg/kg bodyweight respectively The mean weight of the animals at the beginning of experiment was 140 8 g at the end 168 3 g with negligible differences between the 3 groups The rate of apposition at measuring point 2 was studied during an 8 day and a 4 day interval following the injections of OTC No significant difference in appositional rate was found between the 3 groups A corresponding experiment was made on 24 adult animals divided into 3 equal groups Mean weight at beginning of the experiment 265 3 g and at the end 272 4 g with negligible differences between the groups Neither in this experiment were any significant differences found in appositional rate The results are based upon 141 observations from 10 animals in the 2 groups given 1 0 mg OTC/kg bodyweight 293 observations from 15 animals in the 2 groups given 10 0 OTC/kg bodyweight and 259 observations from 14 animals in the 2 groups given 20 0 mg OTC/kg bodyweight

It was also noted that when the lowest dosage (1 0 mg/kg bodyweight) was employed the bands were fainter and more difficult to recognise and the frequency of missing bands was higher The dosage of OTC employed for the experiments proper was thought convenient and not to have any appreciable effect on the rate of apposition of dentine

Technique

In each category the injections were given at the same time of the day with a few minutes deviation

An intraperitoneal injection of a tetracycline compound will produce a fluorescent mark in calcified tissues within 30 minutes (Milch et al 1957 Lofgren Nylen & Omnell 1965) Storey (1963) found tetracycline induced fluorescence in enamel 15 minutes after an intraperitoneal injection and Johnson (1966) found fluorescence at the dentine predentine junction within minutes after the injection but did not say how the injections were given It may be assumed that the absorption starts very soon after an intraperitoneal deposition that the accumulation in tissues undergoing calcification follows in close succession and consequently that the marking in the tissue corresponds well to the time of the administration

prising the number of the measuring point the number of the animal right or left side interval and section As the intervals were not of equal length distances found for the 4 day intervals in sets 3 4 5 and 6 had to be doubled This was made by a specially designed program A list of the cards was made

To study the variations in dentine apposition between animals sections and measuring points and their interactions analysis of covariance was carried out Program BMD 03V (IBM) analysis of covariance version of Feb 19 1964 University of Utah Computer Center was selected The thickness of the dentine layer was chosen as a covariable to correct for the variation in the locations of the sections and for the possible differences in size of the teeth

Differences found were said to be

highly significant (***) when $P < 0\ 001$
significant (**) when $0\ 001 < P < 0\ 01$
almost significant (*) when $0\ 01 < P < 0\ 05$

The variation in the rate of apposition of dentine was investigated further and described with the aid of program BMD 05R (IBM) polynomial regression *version of April 13 1964 Health Sciences Computing Facility UCLA* Program BMD 05R can dispose of only 500 measured values This meant that when the 10 measuring points together were the subject of the investigation only 10 (set 4—5) or 12 (the other sets) teeth could be investigated simultaneously Arbitrarily the first of the 2 available observations was selected for this analysis For the statistical analyses not performed with the aid of a computer conventional methods were used

SOURCES OF ERROR

Material

Using rats from an inbred stock *standardising their nutritional and* environmental conditions and maintaining these as close as possible to earlier conditions helps to keep the animal material uniform Before and during the experiments weighing and inspection of the animals served as a kind of health control

The adverse effects of OTC on growth were discussed earlier and it was concluded that in view of the smallness of the doses used in the present investigation such effects were surely minimal To investigate

is not a perfect semi circle but a 210° segment of a spiral the planes of the sections deviate from the radius except section 3 This deviation was estimated in the following way It was thought justifiable to disregard the slight spiral form of the upper incisor Assuming the adult tooth to occupy 210° of a circle the following calculations were made From the point P a line was drawn in the way illustrated in Fig 8 where d is the distance between P and the true centre of the circle For the angle marked 15° this holds sin 15°=d r According to the sine theorem for the triangle containing the angle α d sin α=r sin 45° The following deduction is made sin α=sin 45° sin 15° α=10 55° Thus the section cuts the tooth at an angle deviating by 10 55° from the radius and the measured distance will be l=t cos 10 55°=1 017 t (Fig 9) At section 5 where the total height of the dentine layer is roughly 90 units this distance is measured 1 5 units too long The distances between bands rarely exceed 20 units and then the error (0 34 measuring units) can be ignored

The sections may be placed apically or incisally to the intended place on the curvature of the tooth It was thought necessary to compensate for this methodological error It is obvious that the height of the dentine layer increases towards the incisal edge For every section the total height of the dentine layer from the dento enamel junction to the pulp was determined at measuring point 2 The distance was measured twice if necessary 3 times It may seem illogical to use the outline of the pulp chamber as the limit of this distance and not band 5 it having been shown that the distance between a band and

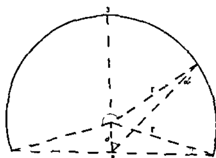


Fig 8

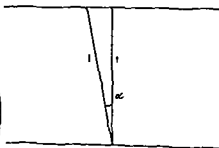


Fig 9

Figs 8 and 9 Drawing showing how deviation of section 5 from radius is estimated

Not every injection of OTC resulted in a fluorescent band. One explanation may be that OTC was deposited in such a place (possibly in the bowel) that very little or no absorption occurred. If only little absorption occurred the fluorescence could be below the visible limit. If the fluorescence is primarily weak but discernible the small amount of fluorophore might be washed away during the fixation or during the preparation of sections and then the bands will not be visible. A possible source of error was to mistake one missing band for another, for example to believe that band 4 was missing when in reality it was band 5. The experimental period was then read as 12 days instead of 8. To avoid this every section was controlled by both observers. Otherwise missing bands were not a source of error.

To investigate whether deep freezing might influence the distances measured a group of animals comprising 6 adult and 4 young rats was investigated. The adult rats were given 2 injections of OTC at a 4 day interval, the young ones according to the usual scheme. The upper incisors were removed immediately after sacrifice. The right one was placed directly into alcohol for fixation and the left one was deep frozen. After an appropriate period of fixation the right incisor was embedded in plastic. The left one was thawed and frozen again 3 times before it was fixed and embedded. Corresponding distances were measured in ground sections of the right and left tooth. The material comprised 190 pairs (right–left) of observations from the adult animals and 100 pairs from the young ones. Sections from 1 to 5 inclusive and all 10 measuring points were represented. Only the first of the double determinations on the right side were compared with those on the left side. The differences between the right and the left teeth were calculated. No significant difference was found between right and left teeth. Normally no significant difference exists between right and left teeth (see page 50). Deep freezing of bone tissue before the preparation of sections for fluorescence microscopy does not diminish the intensity of the fluorescence (Milch et al. 1957, Frost, Roth, Villanueva & Stanisavljevic 1961, Hulth & Olerud 1964). In the present material visual inspection did not reveal any difference in intensity of fluorescence between the left and right teeth.

It is quite clear that the relative crudeness of the method used for determining the positions at which the sections were to be taken implies a fairly large source of error. It is also to be observed that the tooth or a segment of it is not repeatedly divided into 2 equal parts except at the site of section 3 even if the angles are so divided. As the tooth

In what follows apposition of dentine is given in measuring units. If these units were converted to μm it would perhaps give a false impression of accuracy. The precision of the measured values is known but the true value for apposition of dentine is not. When apposition of dentine is later expressed as μm per day this reservation should be borne in mind.

It is possible that the measuring points do not correspond strictly to each other in the different sections. The enamel may perhaps cover a varying part of the circumference of different sections of one and the same tooth and the reference points consequently have a different location. Judging from inspection under the microscope this difference, if any, was small. It was therefore not considered necessary to investigate this matter separately. It was decided to use the method developed and then find out what the variation could be. It was considered probable that at most a comparatively slight shift could occur between the odontoblasts and the dentine they had formed and into which their cell processes passed.

The third measurement was made because the construction of the measuring device favoured faulty readings of about 5 units. These errors are to be regarded as gross errors. As such an attempt to eliminate them was justifiable (Hallert 1967). To estimate the effect of this attempt on the calculations an analysis was made during the course of the investigation. In the category comprising 16 adult normal animals 1400 measurements were made on teeth from the right side and 1420 on teeth from the left side. The third measurement was made in 16 and 20 cases respectively. In young animals treated with growth hormone 2530 measurements were made on teeth from the right side and the third control made in 24 cases. In the analysis of covariance only the variation within replicates was influenced. Investigation showed that it was about 5 per cent "too low".

Statistical analysis

Every calculation and step in the preparation for statistical analysis was made at least twice and the *punching* of cards was controlled. The computer programs must be regarded as adequate and the manual calculations made do not argue against this assumption. The covariable proved to be a small source of error in some of the calculations. When investigating the differences between *intervals* in one section it served the intended purpose. When investigating how a distance varied be-

the pulp was more difficult to measure than that between 2 fluorescent bands It was nevertheless used because it was desired to measure the height of the whole dentine layer The values were not used directly in the estimation of the rate of apposition of dentine but as a more accurate description of the location of the section than its number First an attempt was made to define the section with the aid of the DE pulp distance at point 2 As a trial it was simply assumed that section 1 were those whose dentine height at point 2 varied between 25 and 35 µm The other sections were assigned to appropriately spaced groups The method worked fairly well for sections from the apical parts of the teeth but for those from the incisal parts the overlapping between the DE pulp values was pronounced and using this method would have meant an unnecessary loss of material Instead it was decided to have the DE pulp value as covariable in the statistical analysis this way making a correction

When these DE pulp observations were taken together and scrutinised it was also possible to check that the sections had not been confused for example section 3 mistaken for section 4 This control was possible because it was known that the DE pulp values should be increasing from section 0 or 1 to 5 and 6 for each tooth

If one section of a tooth had a high (or low) DE pulp value the other values for the same tooth were as a rule also high (or low) It seemed that if a section e g the one first cut was placed incisally to the position intended all the others were also placed too near the incisal end and then of course the DE pulp values were higher than they should have been However it appeared that the spaces between the sections were regular If the sections were located too far apically the DE pulp values were lower than the average but — as it seemed — still fairly regularly spaced

Measuring method

Measuring along the dentinal tubules seems convenient as the tubule is described as the path of cellular activity (Herzberg & Schour 1941) It is of course not possible to place the measuring device along a single dentinal tubule It must however be placed more or less parallel to the striation visible in the histologic sections and produced by dentinal tubules (Fig 6) Once the measuring device had been placed in position on a section it was not moved until all distances at the point had been measured

In what follows apposition of dentine is given in measuring units If these units were converted to µm it would perhaps give a false impression of accuracy The precision of the measured values is known but the true value for apposition of dentine is not When apposition of dentine is later expressed as µm per day this reservation should be borne in mind

It is possible that the measuring points do not correspond strictly to each other in the different sections The enamel may perhaps cover a varying part of the circumference of different sections of one and the same tooth and the reference points consequently have a different location Judging from inspection under the microscope this difference if any was small It was therefore not considered necessary to investigate this matter separately It was decided to use the method developed and then find out what the variation could be It was considered probable that at most a comparatively slight shift could occur between the odontoblasts and the dentine they had formed and into which their cell processes passed

The third measurement was made because the construction of the measuring device favoured faulty readings of about 5 units These errors are to be regarded as gross errors As such an attempt to eliminate them was justifiable (Hallert 1967) To estimate the effect of this attempt on the calculations an analysis was made during the course of the investigation In the category comprising 16 adult normal animals 1400 measurements were made on teeth from the right side and 1420 on teeth from the left side The third measurement was made in 16 and 20 cases respectively In young animals treated with growth hormone 2030 measurements were made on teeth from the right side and the third control made in 24 cases In the analysis of covariance only the variation within replicates was influenced Investigation showed that it was about 5 per cent "too low"

Statistical analysis

Every calculation and step in the preparation for statistical analysis was made at least twice and the punching of cards was controlled The computer programs must be regarded as adequate and the manual calculations made do not argue against this assumption The covariable proved to be a small source of error in some of the calculations When investigating the differences between *intervals in* one section it served the intended purpose When investigating how a distance varied be

tween sections the covariable slightly strengthened the variation However analysis showed that when this small error was corrected for there was still a highly significant variation

The sources of error some of which were discussed above contribute to the variation of the observations Estimates of such variations will be given in subsequent chapters

V

NORMAL APPOSITION OF DENTINE

MATERIAL

Four categories of animals were used

1) Adult rats age about 5 months at sacrifice
2) Adult rats age exactly 10 months at sacrifice These animals were reared at the experimental unit and their weights at sacrifice were lower than normal
3) Adult rats age about 11 months at sacrifice They were breeders bought from a breeding centre and their weights at sacrifice were considered normal
4) Young rats age 58 days at sacrifice

RESULTS

Adult animals

Age 5 months

Computer analysis Since the most extensive analysis was performed on data about the 5 month old animals this category will be dealt with first It comprised 25 animals Three could not be used in the computer analysis because fluorescent band 4 was missing The number of animals used in the analyses of the different sets are given in the tables or can be obtained by adding 1 to the number of degrees of freedom for factor T (tooth) The mean weights and weight ranges are given in Table 1 As the animals were not numbered until they were sacrificed the weights of the individual animals were not known until then When the observations had been grouped in the 5 sets covering the 10 measuring points together it was possible to calculate the mean weight for each set right and left side separately The range of the

Table 1 *Mean weights and weight ranges in grams at beginning and end of experiment in different categories of adult female rats*

Day \ Age at end of experiment	Bodyweight (mean and range) adult animals		
	5 mths	10 mths (low weight)	11 mths (normal weight)
0	272 4 250—295	262 2 240—290	335 6 314—360
24	296 0 270—320	276 1 240—310	334 6 294—368

mean weights in these 10 sets was from 286 1 to 297 1 grams on day No 28 For teeth from the right side the mean weights of the animals contributing observations to the analysis of each of the 10 points in each of the 5 sets were calculated The resulting 50 mean weights clustered around the value of 290 grams on day No 28

Analysis of covariance was made for the 5 sets right and left tooth separately The height of the dentine layer at point 2 was used as covariable The results are given in detail in Tables I—II in the Appendix Variations between sections (S) between measuring points (P) and their interaction (SP) were regarded as systematic Variation between animals (=teeth T) was regarded as random variation as were the interactions tooth section (TS) tooth measuring point (TP) tooth section measuring point (TSP) and within replicates (R)

That the different variations can be neglected (null hypothesis no variation) can be investigated with F test The analysis was performed by forming the following quotients for T T TS for S S TS for

Tables 2—3 *Summary of the result of analysis of covariance 5 month old normal female rats*

Table 2

Source of variation	Set 3—4		4—5		
	Right	Left	Right	Left	Right and Left
T	—	—	*	—	—
S	***	***	***	***	***
P	***	**	***	***	* *
TS	***	***	***	***	**
TP	—	—	—	—	—
SP	***	***	***	**	**
TSP	***	***	***	***	* *

Table 3

Source of variation	Set 3 Right	Left	4 Right	Left	5 Right	Left
T	—	—	—	—	—	
I	***	***	*	***	* *	***
P	***	***	*	***	***	**
TI	**	***	***	**	***	***
TI	—	***	*		* *	*
II		***	**	*	* *	* *
TIP	**	**		**		***

P P IP for TS TS TSP for TP TP TSP for SP SP TSP and for TSP TSP R In the analyses of sets 3 4 and 5 the factor section (S) was replaced by factor interval (I) When forming the quotients T TS T TI TS and TI were chosen instead of TP because they were higher than TP Thus a model with variance components was used

For sets 3—4 and 4—5 the results are given in Table 2 All the systematic variations S P SP were considerable A high value for SP meant that the measuring points behaved differently in the different sections Of the variance components T and TI could be ignored because they did not differ significantly from 0 The others differed significantly from 0 and of them TS is to be noted This value meant that although the teeth were similar there was variation between sections This may be explained by the previously mentioned observation that all the sections of a given tooth may be placed too near the apex or the incisal edge The same explanation may apply to TSP If the values found for a given tooth are high in section 2 those for section 5 will be low and vice versa

In sets 3 4 and 5 the systematic variations I P and IP were large (*Table 3*) T could be ignored but the others differed significantly from 0 That TI TP and TIP could not be ignored may be *due to differences* between the positions of the sections in different teeth

To increase the number of animals available for analysis set 4—5 was analysed in right and left teeth taken together Each animal was represented by only one tooth The findings (Tables 1 and 2) were the same as earlier

Having shown the existence of a *significant* variation the next step was to describe the variation more closely

For the 5 sets and the 10 measuring points taken together polynomial regression was performed right and left side separately The purpose

Table 1 *Mean weights and weight ranges in grams at beginning and end of experiment in different categories of adult female rats*

Day \ Age at end of experiment	Bodyweight (mean and range) adult animals		
	5 mths	10 mths (low weight)	11 mths (normal weight)
0	272.4 250—295	262.2 240—290	335.6 314—360
24	296.0 270—320	276.1 240—310	334.6 294—368

mean weights in these 10 sets was from 286.1 to 297.1 grams on day No 28 For teeth from the right side the mean weights of the animals contributing observations to the analysis of each of the 10 points in each of the 5 sets were calculated The resulting 50 mean weights clustered around the value of 290 grams on day No 28

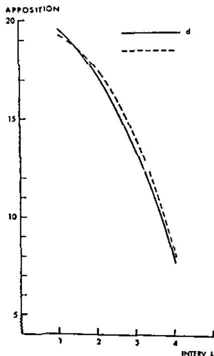
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That the different variations can be neglected (null hypothesis no *variation) can be investigated with F test The analysis was performed* by forming the following quotients for T T TS for S S TS for

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Source of variation	Set 3—4		4—5		
	Right	Left	Right	Left	Right and Left
T	—	—	*	—	—
S	***	***	***	***	***
P	***	***	***	***	* *
TS	***	***	***	***	**
TP	—	—	—	—	—
SP	***	**	***	**	**
TSP	***	***	***	***	***



I ig 14

Fi s 10—14 The calculated variation of dentine apposition for 10 measuring points taken to ether a month old normal rats Fi, 10 set 3—4 Fi, 11 set 4—5 Fig 12 set 3 Fi, 13 set 4 Fig 14 set 5

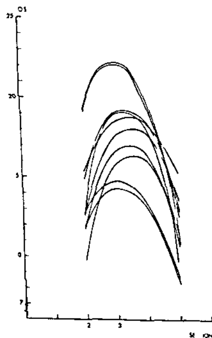


Fig 15

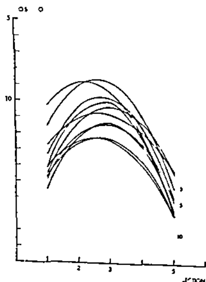


Fig 16

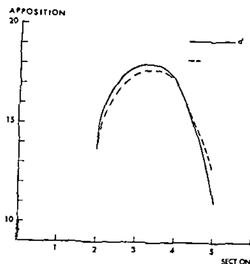


Fig 10

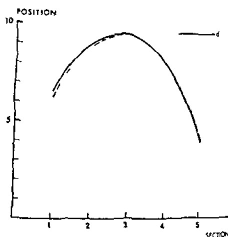


Fig 11

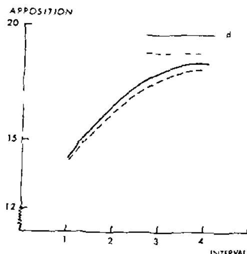


Fig 12

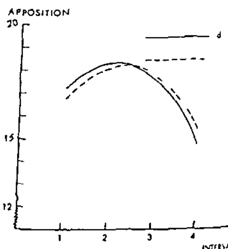
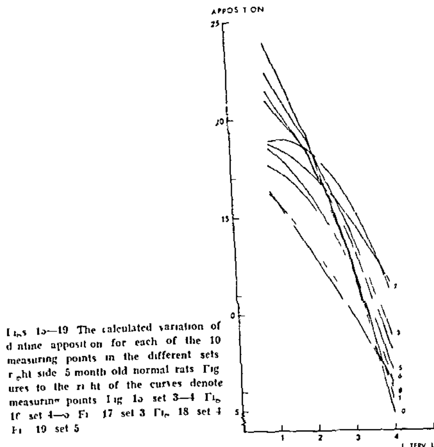


Fig 13

was to describe the variation between sections or intervals with the aid *of a polynomial of the lowest possible degree* A *second degree polynomial* was found suitable With the thickness of the dentine layer as the dependent variable (Y) and interval or section as the independent variable (X) Y was calculated according to the formula

Y = intercept + (1st) regression coefficient X + (2nd) regression coefficient X

The values for Y for 10 measuring points taken together and the number of animals used for calculations in each set are given in Table III and the standard deviations in Table IV The corresponding graphs are *found in Figs 10—14*



Figs 15—19 The calculated variation of dentine apposition for each of the 10 measuring points in the different sets right side 5 month old normal rats Figures to the right of the curves denote measuring points Fig 15 set 3—4 Fig 16 set 4—5 Fig 17 set 3 Fig 18 set 4 Fig 19 set 5

Fig 19

Distances used for the analysis were DE pulp or DE band 5 These were chosen because they seemed to show the greatest variation A mean value was calculated from the 2 replicates Differences were found between animals and between right and left tooth from the same animal too The variation between the right and left teeth was not smaller than that between animals However no systematic difference was found between the right and the left teeth The analysis was also performed for other categories of normal and hormone treated animals with the same results It was therefore considered justified to use the data obtained from both the right and left side in the same animal in the analysis

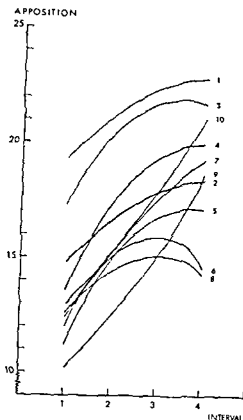


Fig. 17

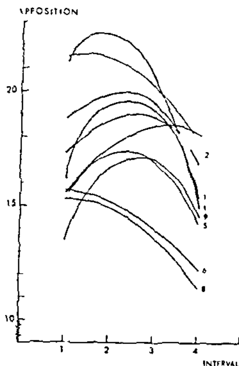
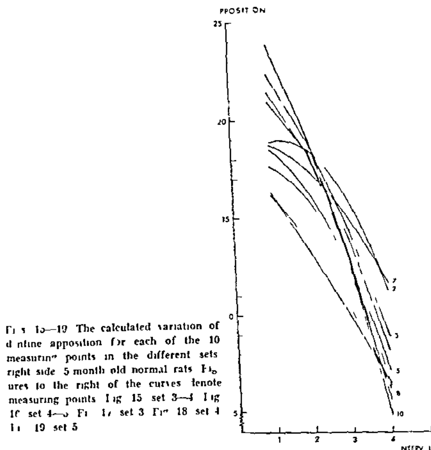


Fig. 18

Polynomial regression was then performed for each of the 10 measuring points in the 5 sets. Because the right and left teeth were found to be similar the calculations were arbitrarily performed for the right side only. *The calculated values for apposition of dentine and the* number of animals on which they were based are given in Table V, the standard deviations in Table VI, and the graphical illustrations in Figs. 15—19.

Extended and simplified analysis. The curves hitherto obtained for the apposition of dentine supported the natural assumption that apposition in the different sets reflected only part of the apposition in the whole tooth. *It was thought desirable to try to make full use of all the* values measured in order to describe the pattern of apposition of dentine as completely as possible. Moreover, the way in which the analysis had hitherto been performed was very time consuming, and a simplified *method would be of value.*

The measured values and the polynomials showed the right and the left teeth to be similar. To confirm this, analysis of variance was made



Figs 15—19 The calculated variation of dentine apposition for each of the 10 measuring points in the different sets right side 5 month old normal rats Figures to the right of the curves denote measuring points Fig 15 set 3—Fig 16 set 4—Fig 17 set 3 Fig 18 set 4 Fig 19 set 5

Fig 19

Distances used for the analysis were DE pulp or DE band 5 These were chosen because they seemed to show the greatest variation A mean value was calculated from the 2 replicates Differences were found between animals and between right and left tooth from the same animal too The variation between the right and left teeth was not smaller than that between animals However no systematic difference was found between the right and the left teeth The analysis was also performed for other categories of normal and hormone treated animals with the same results It was therefore considered justified to use the data obtained from both the right and left side in the same animal in the analysis

As it had became clear that the positions of the sections varied somewhat from tooth to tooth another basis for classification was sought Since the thickness of dentine increases towards the incisal edge it is obvious that the distance from the dento enamel junction to a fluorescent band increases towards the incisal edge If for example *interval 4 is chosen the values measured for this interval can be* arranged according to the distance DE band 4 The higher the latter value the closer the section will be to the incisal edge *For a given* value for DE band 4 the apposition of dentine for the following 4 days was known The DE band values were divided into classes DE band=1 (measuring unit) was the first class DE band=2 was the second class etc These classes were taken into groups of 5 1—5 6—10 and so on

Data on all the 25 animals were used in this analysis The calculations were made without the aid of a computer and could not easily be performed *for every one of the 10 measuring points It was thought* suitable not to make them for the 10 points together As the variation *at point 2 was low this point was selected This analysis was performed* for time periods 8 and 4 days long *i e*, interval 3 and intervals 2 4 and 5 pulp respectively The animals were not of the same age during the different intervals The intervals were compared in pairs The differences between corresponding groups of classes were given different weights depending upon the number of observations added and compared to the standard deviation A comparison between intervals 2 and *4 revealed no significant difference in appositional rate between them* but between intervals 1 and 3 a highly significant difference existed Intervals 2 and 4 were treated together and interval 3 was selected as representative of an 8 day interval For the 4 day intervals it was decided to include the observations in interval band 5 pulp for DE band values higher than 50 Otherwise the values corresponding to high DE band values would have been rather few The use of values measured between a fluorescent band and the pulp chamber *may introduce an* error as the inner border of dentine is difficult to identify A comparison between the observations for interval 4 and band 5 pulp chamber revealed a wider variation among the latter but no significant difference It was thought that the disadvantage of a somewhat wider variation was outweighed by the larger number of values on which to base the curve

Tables VII—VIII *give the number of values in each group of classes* the mean values and the standard deviation for individual values The resulting *graphs are in Figs* 20—21 On the X axis the thickness of the

APPOSITION

20

15

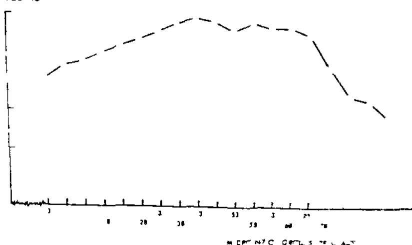
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3 13 23 33 43 53 63 73

8 18 28 38 48 58 68

MIDPOINT OF GROUPS OF CLASSES

Fi 20 The observed variation of dentine apposition at point 2 during an 8 day interval a month old normal rats



F 1 The observe l variation of dent e apposit n at p nt during intervals a month ol l n rmal rat

dentine layer from the dento enamel junction to the actual band is given as values for the midpoints of the groups of classes The corresponding measured values for apposition of dentine during the following 8 or 4 days are given along the Y axis The curve for the 8 day interval is based on 183 observations and that for the 4 day intervals on 499 measured values

During the calculations it was also found that the standard deviations were larger when the values for DE band were high The standard deviations are not given for each group of classes but a border was chosen between the 2 groups with midpoints 48 and 53 (Tables VII—VIII) because the increase of the standard deviations began there

Age 10 months, low weight

This category comprised 9 animals Mean weights and weight ranges are given in Table 1 All the animals are included in the analysis

Analysis of covariance was performed and the details are given in Tables IX—X The same model with variance components was applied

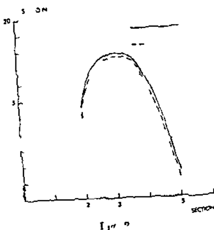
Tables 4—5 *Summary of the result of analysis of covariance 10 month old female rats, low weight*

Table 4

Source of variation	Set 3—4		4—5	
	Right	Left	Right	Left
T	—	—	—	—
S	***	***	***	***
P	***	***	***	***
TS	***	***	***	***
TP	**	—	—	—
SP	***	***	**	***
TSP	***	***	***	***

Table 5

Source of variation	Set 3		4		5	
	Right	Left	Right	Left	Right	Left
T	—	—	—	—	**	—
I	***	* *	***	***	**	**
P	***	***	***	***	**	***
TI	***	***	***	*	***	***
TP	***	***	***	* *	* *	*
IP	***	***	***	* *		**
TIP	***	***	***	**	*	**



I ig ?

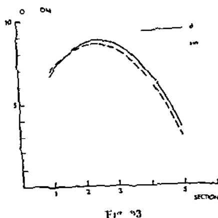
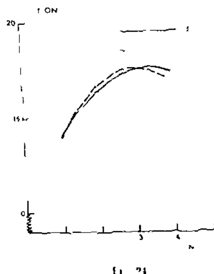
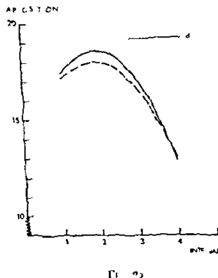


Fig 23



I 24



Fi 25

and the results are in conformity with those obtained for the 5 month old animals (Tables 4—5)

Polynomial regression was performed for the 10 points taken together and the results are given in Tables XI—XII and Figs 22—26. The general picture of apposition of dentine was the same as that obtained earlier. At this stage of the investigation it was not considered necessary to perform "extended and simplified analysis" for this category

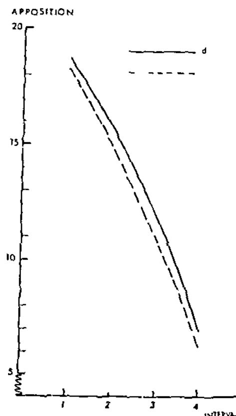


Fig 26

Figs 22—26 The calculated variation of dentine apposition for 10 measuring points taken together 10 month old rats Low weight No treatment Fig 22 set 3—4 Fig 23 set 4—5 Fig 24 set 3 Fig 25 set 4 Fig 26 set 5

Age 11 months

This category comprised 16 animals Mean weights and weight ranges are given in Table 1 Data on 13 were used in the computer analysis

The details of analysis of covariance are given in Tables XIII—XIV and in summary in *Tables 6—7*

Polynomial regression was performed for the 10 measuring points taken together The values for dentine apposition calculated from the polynomial are given in Table XV and the standard deviations in Table XVI The corresponding graphs are Figs 27—31 The pattern of dentine apposition was essentially the same as in the categories investigated earlier

Young animals

This category comprised 27 animals and the mean weights and weight ranges for males *and* females together during the experiment and for females only on day 28 are given in *Table 8 On day 28 the mean* weight for males was 235 9 grams and the range 208—278 The analysis

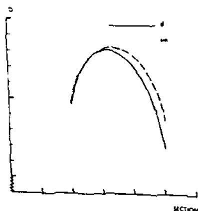
Tables 6—7 *Summary of the result of analysis of covariance 11 month old normal female rats*

Table 6

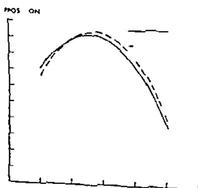
Source of variation	Set 3—4		4—5	
	Right	Left	Right	Left
T	*	—	—	—
S		*	**	**
P	***	**	*	***
TS	* *	*	**	***
TI	*	*	—	*
SP	***	*	**	* *
TSP	***		***	

Table 7

Source of variation	Set 3		4		5	
	Right	Left	Right	Left	Right	Left
T	**	—	—	—	*	**
I	***	*	*	**	*	***
P	*		***	**	**	**
TI	**	***	**		***	***
TP	***	**	*		—	**
II	*	*	**		***	***
TII	**	*	***	* *	* *	***



Fi 7



Fi 78

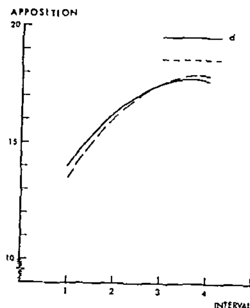


Fig. 29

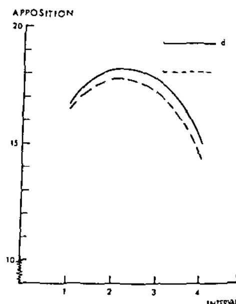


Fig. 30

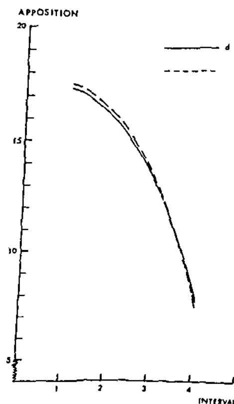


Fig. 31

Figs 2 –31 The calculated variation of dentine apposition for 10 measuring points taken together 11 month old normal rats Fig 2 set 3—4 Fig 28 set 4—5 Fig 29 set 3 Fig 30 set 4 Fig 31 set 5

made with the aid of the computer is based on values obtained for 19 animals in the following analysis data on all 27 animals

Table 8 Mean weights and weight ranges in grams during experiment in different categories of young animals Treatment from Day 13 through 24 The figures for Day 28 (sacrifice) apply to females only otherwise they are given for males and females together Age at beginning of experiment 30 days

Day	Bodyweight (mean and range) young animals		
	No treatment	GH	Solvent for GH
0	8 1 59— 99	86 50—106	83 9 55—119
12	131 0 103—200	140 7 85—194	144 6 104—215
4	184 3 140—242	193 5 121—264	207 1 13 —2 6
28 (females only)	1 5 7 148—188	1 9 7 133—217	174 4 141 – 190

The results of covariance analysis are given in Tables XVII —XVIII The same model with variance components as for the adult animals was applied and the result is given in Tables 9—10 The findings are the same as for the adult animals The factors section interval and measuring point and their interactions are the important ones and their influences are highly significant That factor tooth in one case is significant does not invalidate this statement Concerning the significant interactions the same explanations may apply as to the adult animals

The analysis was carried further and for the 10 points taken together the values measured were fitted to a second degree polynomial The values calculated from the polynomial are given in Table XIX and the standard deviations in Table XX The graphs are in Figs 32—35

The analysis of individual measuring points was performed only for set 4—5 right side The calculated values and the standard deviations are given in Tables XXI—XXII and the graph in Fig 36

In the "extended and simplified analysis" it was found necessary to treat the intervals of equal length separately because it was found that apposition of dentine during intervals 1 and 2 differed systematically and significantly from respectively 3 and 4 The mean values for

Tables 9—10 *Summary of the result of analysis of covariance Young normal female rats Age at beginning of experiment 30 days*

Table 9

Source of variation	Set 3—4 Right	Left	4—5 Right	Left
T	**	*	—	—
S	***	***	***	***
P	***	***	***	***
TS	***	***	***	***
TP	—	—	*	*
SP	***	***	***	***
TSP	***	***	***	***

Table 10

Source of variation	Set 5 Right	Left	6 Right	Left
T	—	—	—	—
I	***	***	***	***
P	***	***	***	***
TI	***	*	**	***
TP	—	—	—	*
IP	***	**	***	***
TIP	***	***	***	***

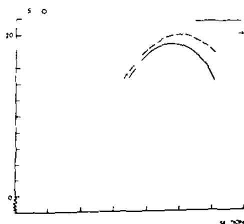


Fig 32

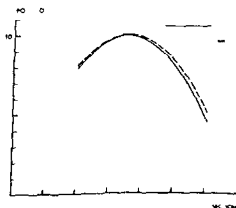
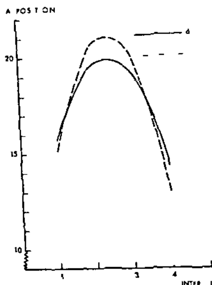


Fig 33



1 34

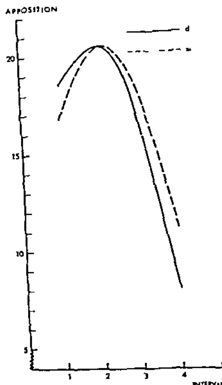


Fig 35

Fi 3—3 The calculated variation of dentine apposition for 10 measuring points taken together Young normal rats Fig 32 set 3—4 Fig 33 set 4—5 Fig 34 set 5 Fig 35 set 6

the different groups of classes the number of observations and the standard deviations for an 8 day and a 4 day interval are given in Tables XXIII and XXIV respectively The corresponding graphs are Figs 37—38

The pattern for dentine apposition in young animals is essentially the same as in adult animals The important exception seems to be that in young animals the course of events is faster This can be seen for example in Fig 34 which should be compared with Fig 14 which illustrates the apposition of dentine in an adult animal In section 5 both describe the events during the 24 day experimental period *In* adults only the decrease in apposition can be seen while in young

Tables 9—10 *Summary of the result of analysis of covariance Young normal female rats Age at beginning of experiment 30 days*

Table 9

Source of variation	Set 3—4 Right	Left	4—5 Right	Left
T	**	*	—	—
S	***	***	***	***
P	***	***	***	***
TS	***	***	***	***
TP	—	—	*	*
SP	***	***	***	***
TSP	***	***	***	***

Table 10

Source of variation	Set 5 *Right*	*Left*	6 *Right*	*Left*
T	—	—	—	—
I	***	***	***	***
P	***	***	***	***
TI	***	*	***	***
TP	—	—	—	*
IP	***	**	***	***
TIP	***	***	***	***

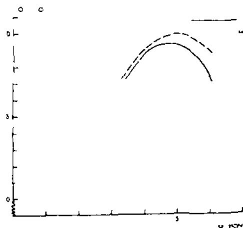


Fig. 32

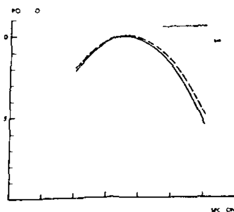
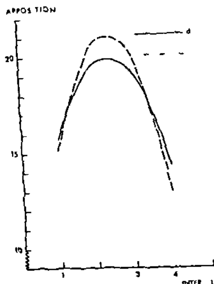


Fig. 33



Fi 34

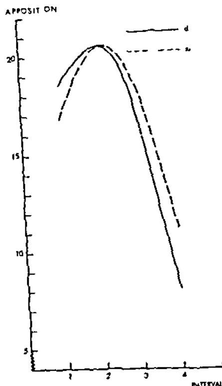


Fig 35

Figs 32—35 The calculated variat on of dentine apposition for 10 measuring points taken together from normal rats Fig 32 set 3—4 Fig 33 set 4—5 Fi 34 et 5 Fig 35 set 6

the different groups of classes the number of observations and the standard deviations for an 8 day and a 4 day interval are given in Tables XXIII and XXIV respectively The corresponding graphs are Figs 37—38

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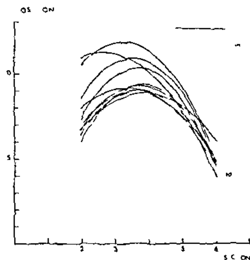


Fig 36 The calculated variation of dentine apposition for each of the 10 measuring points in set 4—5 right side Young normal rats Figures to the right denote measuring points

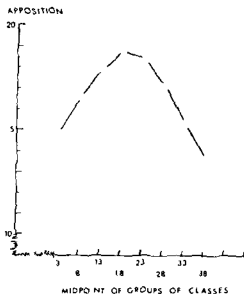


Fig 37

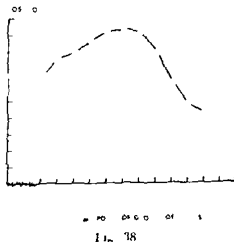


Fig 38

Fig 37 The observed variation of dentine apposition at point 2 during and 8 day interval Young normal rats

Fig 38 The observed variation of dentine apposition at point 2 during a 4 day interval Young normal rats

animals the increase the maximum and the decrease occur during the same period

Determination of the age of the incisor at different levels

It has been shown that the sites of the sections varied somewhat from tooth to tooth and that the effect of this variation was overcome by the use of a different classification It would be of even more value if an age determination could be made

The following calculations were made with the aid of the earlier calculated means of values measured for apposition at point 2 for the 4 day intervals in the adult 5 month old animals (Table VIII) These values had earlier been arranged in groups of classes according to the distance from the dento enamel junction to the peripheral band of these intervals The mean values for the groups of classes were known If the mean value for a group of classes is added to the value for the midpoint of the group the sum denotes the apposition during an unknown time plus 4 days To simplify the analysis distance in measuring units with even figures was chosen With the rule of three the corresponding time in days can be calculated The problem was however that the start of apposition of dentine had to be determined by extrapolation

The reasoning is easier to follow if reference be made to Table 11 The midpoint of the first group of classes was 3 and the mean value for apposition during the following 4 days was 6.57 Then the mean thickness of the dentine layer at the end of these 4 days was 9.57 We selected distance 3—9 When the thickness of dentine increased from 3 to 9 six measuring units were added Since we knew that the apposition of 6.57 units took 4 days it was calculated that apposition of 6 measuring units took 3.65 days For the distance 0—3 it was assumed that the apposition of 6 measuring units took 4 days Then 3 units took 2 days These 2 days are added to the 3.65 days Now we knew that the apposition of 9 units starting from 0 took 5.65 days This procedure was used for the following groups of classes and the result is given in Table 11 The standard deviations of these age determinations were calculated (Table 11)

From the abovementioned it follows that the Y axis in Figs 20—21 (page 58) and 37—38 (page 63) may also denote time because the height of the dentine layer is related to time

However it should be remembered that these age determinations

Table 11 *Age determination (in days) of different parts of the incisor 5 month old normal rats Value in italics is extrapolated*

Midpoint of groups of classes	Mean apposition	Groups selected (in measuring units)	Duration in days for groups selected	Distance from dento enamel junction in measuring units (left column) and corresponding age in days (right column)		SD (age)
3	6.57	3—9	3.65	3	*2.0*	—
8	7.33	9—14	2.73	9	5.7	0.1
13	7.46	14—19	2.68	14	8.4	0.1
18	7.87	19—24	2.54	19	11.1	0.1
23	8.30	24—30	2.89	24	13.6	0.1
28	8.61	30—35	2.32	30	16.5	0.1
33	8.96	35—40	2.23	35	18.8	0.1
38	9.38	40—45	2.13	40	21.0	0.1
43	9.67	45—50	2.07	45	23.2	0.1
48	9.47	50—55	2.11	50	25.2	0.1
53	9.00	55—60	2.22	55	27.4	0.1
58	9.16	60—65	2.18	60	29.6	0.1
63	9.12	65—70	2.19	65	31.8	0.1
68	*9.05*	70—75	*2.21*	*70*	*33.9*	*0.1*
73	8.67	75—80	2.31	75	36.2	0.2
78	6.96	80—84	2.30	80	38.5	0.2
83	5.61	84—88	2.85	84	40.8	0.2
88	5.39	88—93	3.71	88	43.6	0.2
93	4.57	93—97	3.50	93	47.3	0.3
				97	50.8	0.5

are derived from observations of apposition at point 2 and are only valid for this point Another limitation is that the beginning of apposition of dentine was determined by extrapolation

SOURCES OF ERROR

The choice of systematic and random variations in the model for analysis of covariance may be regarded as well founded The variations between sections intervals measuring points and their interactions are primarily the topic of the investigation The F test showed that in a selected group of animals the variations between animals (T) were negligible compared with other variations studied This is in accordance with general biological principles in experimental investigations

Concerning the choice of a suitable degree for the polynomial it was thought that the second degree would fit most cases To check this the F test was carried out and for different categories of normal animals it was found that a second degree polynomial was satisfactory

This can also be shown by comparing the values measured for dentine apposition with those calculated with the aid of the polynomial Table XXV gives the means of measured values at each of the points in the different sets for the 5 month old normal adult animals right side On comparison of these values with the corresponding *calculated* values in Table X good agreement will be found A curve of the third and fourth degree can always be adapted to 4 and 5 measured values respectively From a biological point of view a function of the second degree seems to be natural and logical It was then decided to describe the apposition of dentine as a second degree polynomial

As it had been proved that highly significant differences existed between measuring points it was natural that the variations of the adapted curves were less for the individual points than for the points taken together Tables IX and XI Among the individual points 2 was the one with the least variation *i e* standard deviations for this point generally had the lowest values This was shown for the different sets in the category of adult 5 month old animals For the young ones it was calculated only for set 4—5 right side Experience showed that measuring at point 2 was comparatively easy regardless of the age of the animals It was therefore not considered necessary to make a complete computer analysis for all sets in young animals Nor was it considered necessary to make this analysis for the older adult animals at this stage of the investigation

The limitations of the age determinations of the incisor were mentioned in the description of the method The standard deviations given describe the uncertainty of the mean values for apposition The variation depending upon the systematic errors such as assumption of linear apposition of dentine and the selection of groups for the age determination are not included This latter variation is hard to estimate but is probably not greater than the variation given

DISCUSSION

Three phases could be recognised in the curve *for the rate* of apposition of dentine a rising one a maximum one and a falling one The result was the same whether it was based on measurements made during a given time interval in *different* sections or during different time intervals in sections The general pattern was the same whether the curves were based on the values *noted* at a single measuring point or the 10 measuring points were combined to a "mean" measuring

point In the former case there were obvious differences between the different points with regard to the magnitude of the measured values and also with regard to the occurrence of the maxima of apposition (Figs 15—19 36, pages 49—51 and 62) When all the measured values from point 2 were exploited for the investigation of the appositional rate as described in the simplified analysis again the same pattern emerged

Thus when 3 different methods were used for the analysis the same picture of dentine apposition was obtained in 4 experimental categories of animals

Though it appeared improbable that a fundamental methodological error was the cause of the variation found the method for taking histologic sections may again be touched upon Sections with number 3 were those closest to the radius of the tooth and the values for dentine apposition in these sections ought to be closest to the true values Sections from the apical and incisal parts deviated from the radius and the values found for apposition of dentine were 'too large The values measured and accounted for previously however showed the opposite pattern The conclusion can be drawn that the deviation of the sections from the radius counteracts rather than contributes to the variation *found in apposition of dentine In the statistical investigation of the* variation between intervals in one and the same histologic section deviation of the section from the radius has no effect on the proportions between the intervals That observations at point 2 were selected for the simplified analysis may to some extent have reduced the error connected with the cutting of segments In one plane a possible rotation of the section may occur round an axis roughly corresponding to the place where measurements at point 2 are performed and if this occurs the measured values are affected little or not at all by this error

The conclusion may be drawn that there are good reasons to assume *that the variation in the rate of apposition of dentine found* and described is true and not simply apparent Even visual inspection of the histologic sections shows a variation (Figs 39—43)

Schour and co workers (page 17) who investigated this subject did not describe this variation in apposition of dentine and this may at least partly be attributed to their technique A survey of their reports shows that they used both transverse and sagittal sections from the incisors for measurements *but — as far as can be seen — they used* only 1 transverse section per tooth The technical difficulties in making longitudinal sections may explain why the variation was not discovered in these It is also impossible to know with certainty from



Fig 39

Figs 39—43 Microphotographs of sections 1—5 from an 11 month old normal animal Fig 39 section 1 4 fluorescent bands (2—5) visible Fig 40 section 2 4 fluorescent bands (2—5) clearly visible band No 1 is discernible under the enamel (top of the picture) Figs 41—43 sections 3 4 and respectively Five fluorescent bands visible 37×

their reports where on the circumference of the tooth the measurements were made Weinmann (1942) mentioned differences similar to those reported above but he thought them to be due to the toxicity of his marking substances

A search of the literature revealed no reports indicating that the variation of dentine apposition in the white rat s upper incisors has ever been so closely described as in the present investigation

When the pattern of apposition of dentine was compared in the 3 categories of animals of different ages and normal weights it was found that young animals differed considerably from adult animals The course of events was much faster in young animals (Figs 19 and 34 pages 51 and 61) In young animals apposition during intervals 1 and 2 differed highly significantly from that during intervals 3 and 4 respectively The difference may perhaps be explained by the quicker development of the animals at this age Consequently the different ages

Fig 40

Fig 41

Fig. 42

Fig. 43

Fig. 40

Fig. 41

Fig. 42

Fig. 43

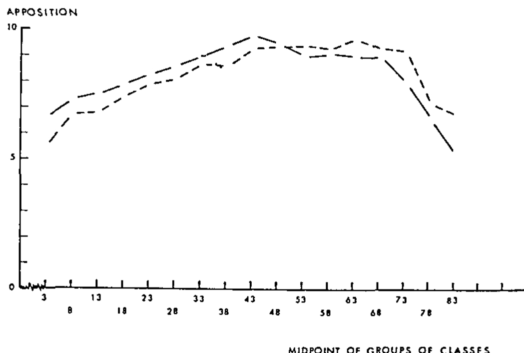


Fig 44 Dentine apposition in normal animals of different ages Y axis mean value from 4 day intervals 2 and 4 X axis midpoints of groups of classes (=age of the formative cells) o — o — o 5 month old animals o o o 11 month old animals o o o young animals

of the animals during different intervals affects dentine apposition more in young animals than in adults

In the 2 categories of adult animals of normal weight age about 5 and 11 months respectively the differences in pattern of apposition were much smaller despite a comparatively larger difference in age (Fig 44) The 10 month old animals of low weight differed somewhat from those with normal weight During the increase in rate of apposition of dentine the difference was small but the maximum occurred somewhat earlier and was not of the same magnitude as in the animals with normal weight and the decrease was somewhat more rapid

The age determinations were founded on observations made at point 2 and are valid only for this point They are based upon the formation of dentine They cannot forthwith be used to describe the chronological age of the odontoblasts corresponding to point 2 but denote the "functional age" of these odontoblasts It is true that the difference may be small but the distinction ought to be made With the method described age determinations can be made for any point if the laws of growth

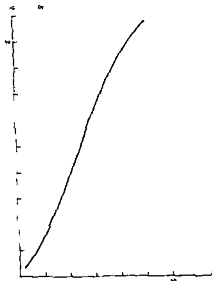


Fig. 45 Height of the dentine layer (Y axis) versus incisor age in days (X axis) 3 month old normal animals (cf Table III)

of the incisor are to be analysed further For this investigation no such further analysis was necessary

If desired the appositional rate in μm per day can be calculated by multiplication of the figures given by 10 and division by the actual interval in days (4 6 or 8) If it is made for sections 3 point 2 in 3 month old animals with the aid of values calculated from the poly nomial (Table V) it will be found that the mean rate increases from 18 5 μm during interval 1 to 23 0 μm during interval 4 Much greater differences can be found for other measuring points and other sections

If the curve for height of the dentine layer versus time (Fig 45) is studied a slight but discernible S form can be found This S form though more marked is found in curves describing other types of growth such as weight in relation to age of the rat (Zucker Hall Young & Zucker 1941 Zucker & Zucker 1942) the number of individuals in relation to age in a population and weight in relation to age of indi viduals (Brody 1945) Thus the growth of incisor dentine is in agree ment with some other types of growth

The comparison between the formation of 2 types of calcified tissues dentine in the rat incisor and bone in an osteone may be of interest Jee & Arnold (1954) using Ca^{45} as a tracer found that the rate

of bone apposition in a Haversian system was highest during the first half of the formation process Marshall Jowsey & Rowland (1959) made similar findings Lee (1964) studied the bone formation rate in osteones with the aid of tetracycline markings and found a linear relationship between appositional growth rate and diameter of the marker However he admitted that at the lower rates of growth the correlation was not so good Frost (1964) described the rate of bone formation in a Haversian system by means of an S shaped curve based on a histogram

It is possible that different forms of growth can be described by S shaped curves As measurement at low rates of growth may be difficult the values forming the basis of the 2 ends of the curve may be difficult to obtain If a method does not allow measurement of low rates of growth it will record only the fairly linear part of the curve This may explain the discrepancies between the findings by different authors regarding Haversian systems

VI

APPOSITION OF DENTINE UNDER INFLUENCE OF PITUITARY GROWTH HORMONE AND OF HYDROCORTISONE

INTRODUCTION

The purpose of this study was to find out whether administration of either of the hormones had any effect on the rate of growth of dentine. The growth hormone was studied for its effect on both adult and young animals, hydrocortisone only on adult animals.

CHOICE OF HORMONE PREPARATIONS

Growth hormone can be obtained from different sources. The porcine growth hormone preparation Somacton has previously been used in investigations in man and experimental animals.

Carstensen, Paulsen & Rudberg-Roos (1955) gave Somacton and insulin to patients with advanced pulmonary tuberculosis and in 8 cases they found "definite improvement of the general condition in all but one patient and a weight increase in all but two cases". Saikku (1956) found Somacton to have a maturing effect on granulation tissue and to increase the tensile strength of healing experimental wounds. Brummer (1966) studied the formation of adhesions around a traumatised tendon and found Somacton to accelerate the formation of collagen.

Somacton has been reported to accelerate healing of fractures of the tibia in the rat (Koskinen 1959). Given in combination with thyrotropin it is said to promote fracture healing in humans (Koskinen 1963).

It was decided to use this preparation of growth hormone[1] because it was fairly readily available and second because it has been reported to have positive effect also on the formation of mineralised tissue.

[1] Generously supplied by AB Ferrin, Malmo

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It is possible that different forms of growth can be described by S shaped curves As measurement at low rates of growth may be difficult the values forming the basis of the 2 ends of the curve may be difficult to obtain If a method does not allow measurement of low rates of growth it will record only the fairly linear part of the curve This may explain the discrepancies between the findings by different authors regarding Haversian systems

i.e. 5 or 10 I.U. GH, it was decided to give 10 I.U. of GH daily to adult animals and 2 I.U. daily to young animals, which doses are well above those used by Koskinen (1959).

The supply of hydrocortisone could be regarded as unlimited. In young rats Johannessen (1964) found oral administration of cortisone to retard dentinogenesis in the molars. The dose is not expressed in mg per kg bodyweight but, judging from the figures given, it varied between 17 and 40 mg/kg bodyweight. Follis Jr. (1951) found 20 mg cortisone acetate per kg bodyweight to have no effect on the epiphyseal cartilage in the rat. Profound disturbances occurred when the dose was 40 or 50 mg. Stanisavljevic et al. (1962) found a daily dose of 1 mg hydrocortisone acetate to retard lamellar bone formation. In the present investigation it was decided to give a daily dose of 25 mg (vol. 1 ml) hydrocortisone, i.e. a very large dose.

The doses of GH and hydrocortisone were not intended to be comparable.

ROUTE OF ADMINISTRATION

According to Greenspan et al. (1949) the effect of GH investigated by the tibia test is the same whether the hormone is given subcutaneously, intraperitoneally or intravenously. It was decided to give GH subcutaneously to the adult animals and to reserve the intraperitoneal route for the suspension of hydrocortisone acetate in case it should be desired later to give the two hormones simultaneously. Because of the smallness of the young animals it was easier to inject GH intraperitoneally. Hydrocortisone has been reported to be effective when given intraperitoneally (Stanisavljevic et al. 1962).

MATERIAL AND METHODS

Adult animals

Two series of experiments, primary experiments and control experiments were performed.

Primary experiments

Thirty-two female rats were divided into 2 equal groups. One group was given a daily intraperitoneal injection of 25 mg (1 ml) hydrocortisone acetate and the other a daily subcutaneous injection of 10 I.U. porcine GH (1 ml) on the last 12 days of the earlier used experimental period corresponding to intervals 3 and 4. At end of the experiment the

The hormone was delivered in vials containing 50 I.U. of GH (in dry substance). Before use it was dissolved in 5 ml of solvent. The solvent consisted of distilled water containing 5 per cent glucose and 0.5 per cent phenol. With the aid of hydrochloric acid the pH was adjusted to 3—4.

Stanisavljević et al. (1962) reported that hydrocortisone acetate retarded lamellar bone formation more than cortisone acetate. In their study of callus formation Hulth & Olerud (1964) used cortisone acetate (Cortodrin® Astra) which was found to retard bone repair. The same manufacturer's preparation of hydrocortisone acetate (Hydrocortodrin® Astra)[2] was used in the present investigation.

It is a suspension containing 25 mg of hydrocortisone acetate (17-hydroxycorticosterone-21-acetate) per millilitre. The suspension medium used in the control experiments was supplied by the manufacturer.[3] It contains Tween 80, phenylcarbinol, carboxymethylcellulose, sodium chloride and distilled water.

The descriptions of the hormones, the solvent and the suspension medium have been obtained from the manufacturers.

DURATION OF HORMONE TREATMENT

It was intended to study dentine formation before and during hormone treatment in one and the same animal. The duration of hormone treatment was selected so that the earlier used investigation period (24 days) was divided into 2 parts. In the beginning and without knowledge of the effect of the above hormones on dentine formation it seemed natural to use a control period of the same length as the period of treatment. It was considered self-evident that the control period should precede the hormone period.

DOSAGE

It was decided to use such large doses that a lack of response could not reasonably be ascribed to too small a dose.

When deciding upon the dose of GH it had to be taken into account that the supply was not unlimited and that the protein solution might cause local irritation. If such a reaction occurred it might interfere with the result. When choosing between 1/2 and 1 millilitre of solution

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[2] Generously supplied by AB Astra, Södertälje.

RESULTS

Effect of growth hormone

Adult animals

Primary experiments The weights of the animals during the experiment are given in Table 12 On day No 28 the mean weights of the animals in the different sets ranged from 283 0 to 293 7 grams

The computer analysis is based on values from 12 animals and the simplified analysis on values from 16

The results of analysis of covariance are given in Tables XXVI—XXVII and summarised (page 46) in Tables 13—14 It is seen that the factors S I and P and their interactions are the chief sources of variation To the exceptions the same explanations may apply as by the normal animals

The statistical analysis was carried further to include polynomial regression This was based on the means of the values recorded for the 10 measuring points in each of the sets right and left side separately and for each of the points in the sets on the right side Analysis with the aid of F test revealed that apposition could be satisfactorily described with a second degree polynomial The calculated values for apposition of dentine the number of animals and the standard deviations are given in Tables XXVIII—XXXI If these values are compared with the corresponding values in normal 5 month old animals (Tables III and V) a general pattern will emerge The rate of dentine apposition in the GH treated animals was as a rule lower than in the untreated animals during the period before hormone treatment but during this treatment it rose and was finally higher This finding was the same whether the values were analysed for each measuring point separately or whether the values formed at all 10 points were pooled before analysis This means that this investigation failed to show that dentine formation corresponding to any particular measuring point is

Table 12 *Mean weights and weight ranges in grams during experiment 4 month old animals Treatment with growth hormone during latter half of experimental period Primary experiments*

Day	0	1[illegible]	21	[illegible]8
Mean weight	[illegible] 1	[illegible]3[illegible]	[illegible]1 [illegible]	[illegible]1 [illegible]
Range	[illegible]— [illegible]0	[illegible]10—2[illegible]	[illegible]—31[illegible]	[illegible]4—310

animals were a little more than 4 months old. The different techniques used were the same as those described in Chapter IV.

Control experiments

One hundred female rats were divided into 5 equal groups of practically the same mean body weight. The cages were randomly distributed in the stable. Five injections of OTC were given at *6 day intervals*; otherwise the animals were treated in the way described earlier. Intervals of equal length were used to facilitate the simplified analysis. At the end of experiment the animals were slightly above 4 months.

Of those 100 animals, group 1 served as untreated controls, while the other 4 groups received various injections:

1) No treatment.
2) Daily subcutaneous injection of 10 I.U. (1 ml) of porcine GH during the last 12 days of the experimental period.
3) Daily subcutaneous *injection of 1 ml solvent for GH during the last* 12 days of the experimental period.
4) Daily intraperitoneal injection of 25 mg *(1 ml) hydrocortisone* acetate during the last 12 days of the experimental period.
5) Daily intraperitoneal injection of 1 ml of the suspension medium for hydrocortisone acetate during the last 12 days of the experimental period.

The previously described histologic and measuring techniques were used with the exception that measurements were made only at measuring point 2 and always by the author personally. When making the measurements the author did not know to which group of animals a given histologic section belonged. Some of the observations were checked by the *technical assistant in randomly selected sections*.

Young animals

Forty five animals received daily intraperitoneal injection of 2 I.U. GH and 17 the corresponding volume (0.2 ml) of solvent for GH during the last 12 days of the experimental period. Age at beginning of experiment 30 days.

RESULTS

Effect of growth hormone

Adult animals

Primary experiments The weights of the animals during the experiment are given in Table 12 On day No 28 the mean weights of the animals in the different sets ranged from 283 0 to 293 7 grams

The computer analysis is based on values from 12 animals and the simplified analysis on values from 16

The results of analysis of covariance are given in Tables XXVI—XXVII and summarised (page 46) in Tables 13—14 It is seen that the factors S I and P and their interactions are the chief sources of variation To the exceptions the same explanations may apply as by the normal animals

The statistical analysis was carried further to include polynomial regression This was based on the means of the values recorded for the 10 measuring points in each of the sets right and left side separately and for each of the points in the sets on the right side Analysis with the aid of I test revealed that apposition could be satisfactorily described with a second degree polynomial The calculated values for apposition of dentine the number of animals and the standard deviations are given in Tables XXVIII—XXXI If these values are compared with the corresponding values in normal 5 month old animals (Tables III and V) a general pattern will emerge The rate of dentine apposition in the GH treated animals was as a rule lower than in the untreated animals during the period before hormone treatment but during this treatment it rose and was finally higher This finding was the same whether the values were analysed for each measuring point separately or whether the values formed at all 10 points were pooled before analysis This means that this investigation failed to show that dentine formation corresponding to any particular measuring point is

Table 12 *Mean weights and weight ranges in grams during experiment 4 month old animals Treatment with growth hormone during latter half of experimental period Primary experiments*

Day	0	[illegible]	[illegible]	28
Mean weight	[illegible]	[illegible]	291 4	291 [illegible]
Range	[illegible]	[illegible]	[illegible]—316	[illegible]—310

Tables 13—14 *Summary of result of analysis of covariance 4 month old animals Treatment with growth hormone during latter half of experimental period Primary experiments*

Table 13

Source of variation	Set 3—4 Right	Left	4—5 Right	Left
T	—	—	—	—
S	***	***	***	***
P	***	***	***	***
TS	***	***	***	***
TP	—	—	—	**
SP	***	***	***	***
TSP	***	***	***	***

Table 14

Source of variation	Set 3 Right	Left	4 Right	Left	5 Right	Left
T	—	—	—	—	—	—
I	***	***	**	*	***	***
P	***	***	***	***	***	***
TI	—	***	***	***	***	***
TP	—	***	**	***	—	**
IP	***	***	***	***	***	***
TIP	***	***	***	***	***	***

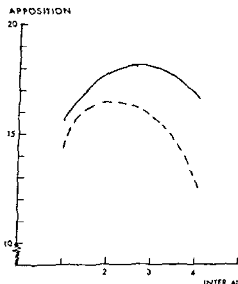


Fig 46 Calculated variation of dentine apposition Set 4 10 measuring points taken together ——— 5 month old normal animals — — — 4 month old animals treated with growth hormone during latter half of experimental period 4 month old animals treated with cortisol during latter half of experimental period Primary experiments

more susceptible than others to GH To save space it was not considered necessary to illustrate the findings graphically so completely as in the normal animals A representative curve for normal apposition and for comparison the corresponding curve for animals under the influence of GH are given in Fig 46 from which it is clear that the 2 curves are very similar in shape they are only somewhat apart This interspace may reflect a true difference between the 2 categories of animals but it may also depend upon an altered rate of eruption or a systematical error in the positions of the sections

The findings were analysed by the simplified method Apposition during both an 8 day (3) and a 4 day (4) interval in a month old untreated animals was compared with that during the corresponding intervals in animals treated with GH No significant differences were found

When the two 8 day intervals were compared with each other in the same category of animals it was found that in the untreated animals there was a highly significant decrease of the rate of dentine apposition during interval 3 compared with that during interval 1 but no such difference was found in the GH treated animals

When the two 4 day (2 and 4) intervals were compared with each other in the normal category and in the category of GH treated animals it was found that in the normal animals the rate of apposition of dentine tended to be somewhat lower during interval 4 than during interval 2 but the difference was not significant In the GH treated animals the rate of dentine apposition was higher during interval 4 when the animals were given GH than during interval 2 when no treatment was given The difference was almost significant

Control experiments The mean weights and weight ranges are given in Table 15 The data were analysed by the simplified method and the numbers and means of the measuring values for untreated GH treated and solvent treated animals are given in Tables XXXII—XXXIV This analysis is based on values from all the animals In the analysis only the mean values for the groups of classes with midpoints from 3 to 38 inclusive were used because these groups showed the least variation around mean values The standard deviations in the different categories were close to each other and for the calculations one and the same estimate 0 8 was used The standard deviation of mean values was calculated by dividing 0 8 by the square root of the number of observations (n)

Comparison of pairs of categories of animals (no treatment versus treatment with GH treatment with GH versus treatment with solvent

Tables 13—14 *Summary of result of analysis of covariance 4 month old animals Treatment with growth hormone during latter half of experimental period Primary experiments*

Table 13

Source of variation	Set 3—4 Right	Left	4—5 Right	Left
T	—	—	—	—
S	***	***	***	***
P	***	***	***	***
TS	***	***	***	***
TP	—	—	—	**
SP	***	***	***	***
TSP	***	***	***	***

Table 14

Source of variation	Set 3 Right	Left	4 Right	Left	5 Right	Left
T	—	—	—	—	—	—
I	***	***	**	*	***	***
P	***	***	***	***	***	***
TI	—	***	***	***	***	***
TP	—	***	**	***	—	**
IP	***	***	***	***	***	***
TIP	***	***	***	***	***	***

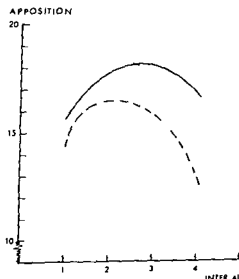


Fig 46 Calculated variation of dentine apposition Set 4 10 measuring points taken together 5 month old normal animals ——— 4 month old animals treated with growth hormone during latter half of experimental period - - - 4 month old animals treated with cortisol during latter half of experimental period Primary experiments

differences were found The difference between intervals 1 and 2 cannot be satisfactorily explained It may be due to chance

In animals treated with GH no difference was found between intervals 1 and 2 The rate of apposition of dentine was highly significantly greater during interval 3 than during 2 and highly significantly *lower* during interval 4 than during interval 3

In animals given solvent for GH no significant differences were found between the intervals

The results are illustrated in Fig 47

Young animals

The mean weights and ranges are given in Table 8 (page 59)

Since extensive analysis of covariance had been performed for normal adult animals normal young animals and hormone treated adult animals and shown the same general pattern it was not considered necessary to perform this analysis for every set of the GH treated young animals It was thought sufficient to perform it for sets 4—5 and 6 right side i e one interval in different sections and different intervals in one section respectively The choice of the right side was arbitrary and consistent with the earlier choice of the right side for certain statistical calculations The detailed results are given in Table XXXV and in summary in Table 16 The findings agree well with those made earlier

Polynomial regression was performed for the above mentioned sets Also in this category of animals apposition of dentine could be satisfactorily (F test) described with a second degree polynomial The results for all 10 measuring points taken together are given in Table

Table 16 Summary of result of analysis of covariance Young rats treated with growth hormone during latter half of experimental period

Source of variation	Set 4—5 Right	Source of variation	Set 6 Right
T	—	T	
S		I	—
I		I	**
TS		TI	**
TI		TI	
SI	* *	IP	*
TSI		TIP	
e			

Table 15 *Mean weights and weight ranges for different experimental categories. 4 month old animals. Control experiments*

Body weight (mean and range). Adult animals, control experiment

Day	Treatment				
	None	GH	Solvent for GH	Cortisol	Suspension medium for cortisol
0	226 5 207—247	230 1 211—254	229 3 212—254	231 5 211—264	227 8 210—245
12	246 0 222—263	248 1 233—265	244 9 227—271	249 5 228—293	244 4 [illegible]
24	257 9 240—274	300 5 282—314	258 9 240—274	195 8 164—222	254 3 241—275
28	258 1 239—273	291 2 266—314	260 1 238—278	188 4 161—210	259 7 241—281

and no treatment versus treatment with solvent) revealed no significant differences in any of the 4 intervals.

When the intervals were compared with each other in the same category of animals, i.e. 1 versus 2, 2 versus 3 and 3 versus 4, the untreated animals showed a significant increase in the rate of apposition of dentine during interval 2 compared with interval 1. Otherwise no

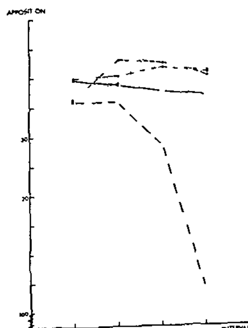


Fig. 47. Dentine apposition under varying circumstances. 4 month old animals. Control experiments. o — o no treatment; o o o treatment with growth hormone during latter half of experimental period; o — o treatment with solvent for growth hormone during latter half of experimental period; o + + o treatment with cortisol during latter half of experimental period; o — o treatment with suspension medium for cortisol during latter half of experimental period. N.B. Y axis: sums of the observed mean values from groups of classes with midpoints from 3 through 3 irrespective of number of observations.

differences were found. The difference between intervals 1 and 2 cannot be satisfactorily explained. It may be due to chance.

In animals treated with GH no difference was found between intervals 1 and 2. The rate of apposition of dentine was highly significantly greater during interval 3 than during 2 and highly significantly *lower* during interval 4 than during interval 3.

In animals given solvent for GH no significant differences were found between the intervals.

The results are illustrated in Fig. 47.

Young animals

The mean weights and ranges are given in Table 8 (page 59).

Since extensive analysis of covariance had been performed for normal adult animals, normal young animals and hormone treated adult animals and shown the same general pattern it was not considered necessary to perform this analysis for every set of the GH treated young animals. It was thought sufficient to perform it for sets 4—5 and 6 right side, i.e. one interval in different sections and different intervals in one section respectively. The choice of the right side was arbitrary and consistent with the earlier choice of the right side for certain statistical calculations. The detailed results are given in Table XXXV and in summary in Table 16. The findings agree well with those made earlier.

Polynomial regression was performed for the above mentioned sets. Also in this category of animals apposition of dentine could be satisfactorily (F test) described with a second degree polynomial. The results for all 10 measuring points taken together are given in Table

Table 16. *Summary of result of analysis of covariance. Young rats treated with growth hormone during latter half of experimental period*

Source of variation	Set 4—5 Right	Source of variation	Set 6 Right
T	—	T	—
S		I	
A		P	*
TS	*	TI	*
TA	*	TP	**
SA		IP	*
TSA		TIP	*

6

XXXVI and for each of the points in set 4—a right side in Table XXXVII. The corresponding standard deviations are given in Tables XXXVIII and XXXIX respectively. The general pattern is the same as earlier.

The data from normal, GH treated and solvent treated animals were analysed by the simplified method. Comparisons were made only between intervals of equal length, i.e. 1 versus 3 and 2 versus 4. The material is presented in Tables XL—XLII. The groups of classes with midpoints above 38 were not included because of the increase in variation in the higher groups of classes. The standard deviations were estimated at 0.7 for intervals 2 and 4 and at 1.1 for intervals 1 and 3. The standard deviations for the mean values were obtained by dividing these figures by the square root of the number of measuring values (n).

When the 3 categories normal (page 56), GH treated and solvent treated were compared with regard to intervals 1 and 2 (no treatment) it was found that no differences existed between the 3 categories. For this comparison each of the intervals 1 and 2 were compared in the following way: normal versus solvent treated, normal versus GH treated and solvent treated versus GH treated. During intervals 3 and 4 (treatment intervals) the rate of apposition of dentine was highly significantly greater in GH treated animals than in those given solvent but — surprisingly — those animals given solvent had a highly significantly greater rate of apposition than those not treated. The results are illustrated in Fig. 48.

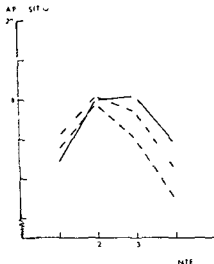
When no treatment and treatment periods were compared with each other in the same category of animals the following results were obtained.

In normal animals there was (as mentioned earlier) a highly significant decrease in the rate of apposition of dentine during intervals 3 and 4 compared with the rate during intervals 1 and 2 respectively.

In animals treated with GH there was no decrease during interval 3 (treatment with hormone) compared with interval 1 (no treatment). The number of observations was, however, comparatively small. The decrease during interval 4 (treatment with GH) compared with interval 2 (no treatment) was also smaller than in the normal animals and was not significant.

In animals given solvent for GH there was a highly significant decrease during intervals 3 and 4 compared with intervals 1 and 2 respectively. Thus the findings were the same as in the normal animals.

The effect of the administration of the preparation of porcine growth



Fi 48 Observed variation of dentine apposition in young animals Those for intervals 2 and 4 have been doubled o o normal animals o —— o animals treated with growth hormone during latter half of experimental period o o animals treated with solvent for growth hormone during latter half of experimental period The curves are comparable only along the vertical axis Cf Tables XI XIII

hormone used here may be *summarised* as follows In adult animals the rate of apposition was highly significantly increased only when the treatment free period was compared with the period of treatment in the same category of animals In young animals an increased rate of apposition was found during the period they were given solvent for growth hormone During the period when growth hormone was given a highly significant increase was detected both within the category of hormone treated animals and when this category was compared with the category treated with the solvent

Effect of hydrocortisone

Adult animals

Primary experiments The weights of the animals are given in Table 17

During the measurements it was found that the outline of the pulp chamber was abnormally wavy and irregular (Fig 49) and it was difficult or impossible to measure the distances between fluorescent bands Already at this stage of the investigation the rate of apposition of dentine appeared reduced

The material available for statistical analysis was less complete than in the other categories The computer analysis was based on values from 8 animals and the simplified analysis on values from 15

Table 17. *Mean weights and weight ranges in grams during experiment. 4 month old animals. Treatment with cortisol during latter half of experimental period. Primary experiments*

Day	0	12	24	28
Mean weight	258.1	256.4	203.5	191.8
Range	240—276	237—273	182—222	180—218

The results of the analysis of covariance (Table XLIII) are summarised in Table 18. In set 4, right side, there was one exception to the earlier rules: the factor interval was not found to be significant and the factor point (P) was only almost significant. Otherwise the results were essentially the same as before.

Polynomial regression was performed for the 10 points taken together. F test showed a second degree polynomial to be acceptable. The results are given in Tables XLIV—XLV. The rate of apposition of dentine was decreased (Fig. 46, page 78). When the individual measuring points were to be analysed it was found that the material being small

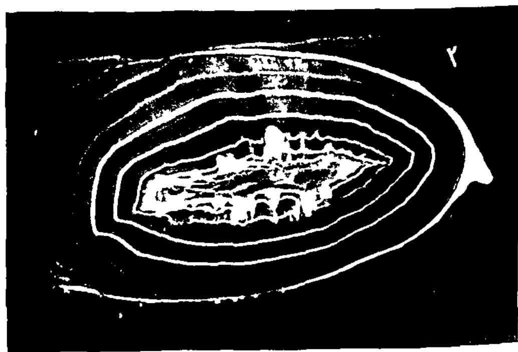


Fig. 49. Microphotograph of section from an animal given cortisol. Control experiments. Observe the wavy and irregular demarcation against the pulpal chamber. 36 ×

Table 18 *Summary of result of analysis of covariance 3 month old rats Treatment with cortisol during latter half of experimental period*

Source of variation	Set 4	5	
	Right	Right	Left
T	—	—	—
I	—	***	**
I	*	*	
TI	**	*	*
TP	—	—	—
II	*		**
TII	**		*

would not allow an analysis for each of the points This analysis was therefore confined to measuring point 2 The results are given in Tables XLVI—XLVII

A *simplified analysis* based upon observations made in 15 animals was performed and when the two 4 day intervals 2 (no treatment) and 4 (treatment with cortisol) were compared it was found that the rate of apposition of dentine was highly significantly *decreased during* cortisol treatment

Control experiments One of the cortisol treated animals died from unknown cause on the third day of treatment The weights are given in Table 15 (page 80)

Simplified analysis was *performed* and the number of observations and the mean values for animals treated with cortisol and for animals treated with suspension medium are given in Tables XLVIII—IL The *results* are based on observations made in all surviving animals In the analysis only the mean values from the group of classes with mid points from 3 including 38 were used because these *groups* showed the least variation The estimated standard deviations were 0 8 and 0 8 respectively

When the animals treated with the suspension medium for cortisol were compared with the untreated animals no difference was found between apposition during intervals 1 and 2 During *intervals* 3 and 4 the animals given suspension medium showed a significant decrease in rate of apposition

When the 4 *intervals in the* category given suspension medium were compared with those in the category treated with CH solvent no significant difference was found for any interval

Table 17 *Mean weights and weight ranges in grams during experiment 4 month old animals Treatment with cortisol during latter half of experimental period Primary experiments*

Day	0	12	24	[illegible]8
Mean weight	258 1	256 4	203 5	191 8
Range	240—276	237—273	182—222	180—218

The results of the analysis of covariance (Table XLIII) are summarised in Table 18 In set 4 right side there was one exception to the earlier rules the factor interval was not found to be significant and the factor point (P) was only almost significant Otherwise the results were essentially the same as before

Polynomial regression was performed for the 10 points taken together F test showed a second degree polynomial to be acceptable The results are given in Tables XLIV—XLV The rate of apposition of dentine was decreased (Fig 46 page 78) When the individual measuring points were to be analysed it was found that the material being small

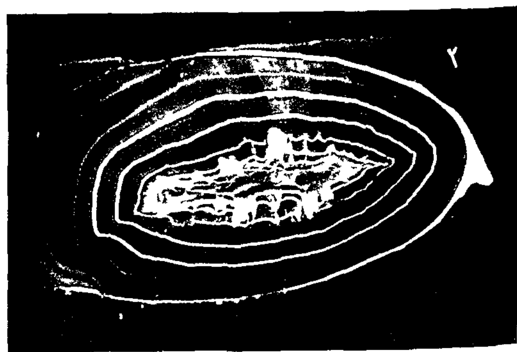


Fig 49 Microphotograph of section from an animal given cortisol Control experiments Observe the wavy and irregular demarcation against the pulpal chamber 3[illegible]×

Table 18 Summary of result of analysis of covariance 4 month old rats Treatment with cortisol during latter half of experimental period

Source of variation	Set 4	5	
	Right	Right	Left
T	—	—	—
I	—	*	*
P			
TI	*	**	* *
TP	—	—	—
IP		***	***
TIP	**	* *	***

would not allow an analysis for each of the points This analysis was therefore confined to measuring point 2 The results are given in Tables XLVI—XLVII

A simplified analysis based upon observations made in 15 animals was performed and when the two 4 day intervals 2 (no treatment) and 4 (treatment with cortisol) were compared it was found that the rate of apposition of dentine was highly significantly decreased during cortisol treatment

Control experiments One of the cortisol treated animals died from unknown cause on the third day of treatment The weights are given in Table 15 (page 80)

Simplified analysis was performed and the number of observations and the mean values for animals treated with cortisol and for animals treated with suspension medium are given in Tables XLVIII—II The results are based on observations made in all surviving animals In the analysis only the mean values from the group of classes with mid points from 3 including 38 were used because these groups showed the least variation The estimated standard deviations were 0 8 and 0 8 respectively

When the animals treated with the suspension medium for cortisol were compared with the untreated animals no difference was found between apposition during intervals 1 and 2 During intervals 3 and 4 the animals given suspension medium showed a significant decrease in rate of apposition

When the 4 intervals in the category given suspension medium were compared with those in the category treated with CH solvent no significant difference was found for any interval

When the cortisol treated animals were compared with those given suspension medium regarding the periods before treatment it was found that apposition during interval 1 in the cortisol treated group was significantly lower than in the solvent treated group while intervals 2 showed no significant difference No satisfactory explanation can be offered for this Anyhow during the 6 day period immediately preceding treatment the 2 categories were without detectable difference When intervals 3 and 4 in the 2 categories were compared it was found that the rate of apposition of dentine was highly significantly lower during hormone treatment than during administration of the suspension medium

When the different intervals were compared with each other in the same category of animals i e 1 versus 2 2 versus 3 and 3 versus 4 no differences were found in the category of animals given suspension medium for cortisol

Animals treated with cortisol showed a highly significantly decreased rate of dentine formation during interval 3 compared with 2 The rate of dentine formation was also highly significantly lower during interval 4 than during 3 (Fig 47 page 80)

Functional age of formative cells and response to hormone

When the analyses were made it was presumed that if the hormones had any effect it would be detectable even if groups of odontoblasts of different ages (=different midpoints of classes) were investigated together The choice of the groups of classes to be included in the analysis was made mainly for statistical reasons A possible refinement would be to investigate the response in each group of classes compared with that in corresponding untreated groups If such a comparison is to be made it should be noted that the only place where treatment is strictly comparable to no treatment is at the transition between the 2 periods in the present investigation between intervals 2 and 3 If the effect of treatment is small compared with the width of the groups of classes selected it can also be made at the transition between intervals 3 and 4 without introducing any error of importance But if the effect of treatment is substantial age will not correspond to the thickness of the dentine layer in the same way as earlier and then the comparison cannot be made or it will have to be corrected for the influence of treatment before the place of comparison

That the influence of treatment can vary with the age of the cells

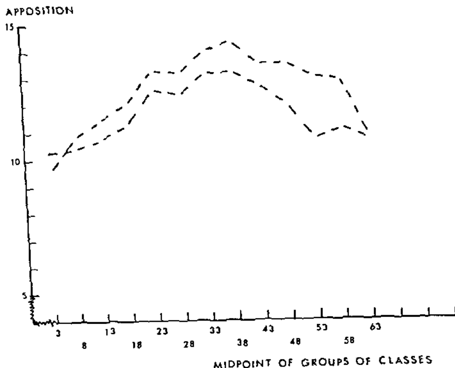


Fig. 50 Observed apposition of dentine during interval 3 (? days control experiment) in normal animals (O— —O) and in animals given cortisol (O—+—O). Those odontoblasts with the highest appositional rate seem to be affected most

is illustrated in Figs 50—51 Fig 50 corresponds to interval 3 and it is seen that those cells with the highest appositional rate seem to be the ones affected most by the administration of cortisol Fig 51 corresponds to interval 4 and the result is the same as earlier only more accentuated and the older cells are also affected The younger ones seem to be more resistant to cortisol

Summarising a retarding effect of the suspension medium was found but in animals given cortisol the rate of apposition of dentine is highly significantly lower during treatment than in normal animals and in those given the suspension medium for the hormone This finding is the same whether the 2 experimental categories are *compared* with each other or treatment and no treatment periods in the cortisol treated categories

When the cortisol treated animals were compared with those given suspension medium regarding the periods before treatment it was found that apposition during interval 1 in the cortisol treated group was significantly lower than in the solvent treated group while intervals 2 showed no significant difference No satisfactory explanation can be offered for this Anyhow during the 6 day period immediately preceding treatment the 2 categories were without detectable difference When intervals 3 and 4 in the 2 categories were compared it was found that the rate of apposition of dentine was highly significantly lower during hormone treatment than during administration of the suspension medium

When the different intervals were compared with each other in the same category of animals i e 1 versus 2 2 versus 3 and 3 versus 4 no differences were found in the category of animals given suspension medium for cortisol

Animals treated with cortisol showed a highly significantly decreased rate of dentine formation during interval 3 compared with 2 The rate of dentine formation was also highly significantly lower during interval 4 than during 3 (Fig 47 page 80)

Functional age of formative cells and response to hormone

When the analyses were made it was presumed that if the hormones had any effect it would be detectable even if groups of odontoblasts of different ages (=different midpoints of classes) were investigated together The choice of the groups of classes to be included in the analysis was made mainly for statistical reasons A possible refinement would be to investigate the response in each group of classes compared with that in corresponding untreated groups If such a comparison is to be made it should be noted that the only place where treatment is strictly comparable to no treatment is at the transition between the 2 periods in the present investigation between intervals 2 and 3 If the effect of treatment is small compared with the width of the groups of classes selected it can also be made at the transition between intervals 3 and 4 without introducing any error of importance But if the effect of treatment is substantial age will not correspond to the thickness of the dentine layer in the same way as earlier and then the comparison cannot be made or it will have to be corrected for the influence of treatment before the place of comparison

That the influence of treatment can vary with the age of the cells

skeletal tissues of intact white rats have been made after long periods of treatment with GH. Baume, Becks & Evans (1954) gave adult rats GH for 436 days and found an increase in tooth size. When Asling & Evans (1961) described the effects on skeletal development of GH in excess to normal growing female rats starting at 81 days of age" they considered administration of GH for 30 days a short term experiment. When studying the induction of gigantism in rats by GH, Asling, Simpson & Evans (1965) administered the hormone for 8 months or more. The period of hormone treatment used in the present investigation, 12 days, was therefore comparatively short. This must be borne in mind in the appraisal of the results.

In *adult animals* the primary experiments indicated that GH had an accelerating effect on dentine formation. In the control experiments the rate of dentine formation was greater during the period when GH was given than during the period without treatment when these 2 periods were compared with each other in the same category of animals. The difference was highly significant when intervals 2 and 3 were compared. However, the increase did not continue during interval 4 but a drop occurred as compared to interval 3. Still, the rate was somewhat higher than during the period with no treatment.

In *young animals* the pattern seems somewhat more distinct. When the apposition in 3 categories, normal, GH treated and solvent treated animals were compared regarding the period preceeding treatment they were found not to differ significantly from one another. When the second parts of the experimental period, i.e. the intervals when treatment was given, were compared it was found that the rate of apposition of dentine in the solvent treated animals was highly significantly greater than in normal animals and that the rate was highly significantly greater in the GH treated animals than in the solvent treated.

When the periods without and with treatment were compared in each category of animals, it was found that both normal and solvent treated animals showed a highly significant decrease in the rate of apposition of dentine during the intervals corresponding to treatment. When the animals were given GH this decrease did not occur and no significant differences were found.

The highly significant difference found between normal and solvent treated animals was unexpected. Several tentative explanations may be offered but no definitive answer can be given. The route of administration may play a role in spite of earlier investigations denying this possibility (Greenspan et al. 1949). It may be due to one or more

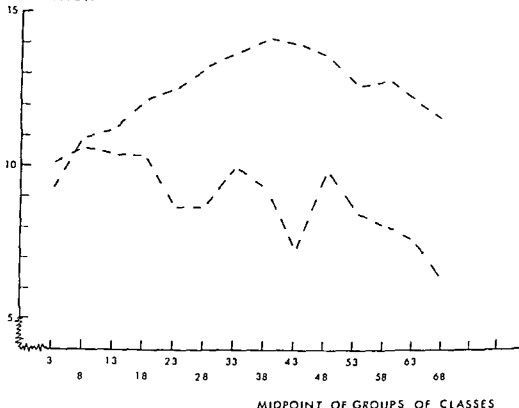


Fig. 31. Interval 4 in the same categories of animals as in Fig. 30. Young cells seem to be affected least.

DISCUSSION

To begin with it should be stressed that the purpose of the experiments was not to make an extensive endocrinological investigation of the effects of GH and cortisol on the rate of incisor dentine formation but simply to find out whether the formation rate could be accelerated or retarded by the administration of hormones (GH and cortisol). As the pattern of apposition was known only for normal animals it was natural to give excessive doses of the hormone to intact animals. The effects of removal of the actual endocrine gland(s) and the effects of substitution therapy would have required investigations of dentine apposition in hypophysectomised or adrenalectomised animals.

Growth hormone

Earlier investigations of the effect of pituitary GH on dental and

vent for GH The suspension medium is more complex than the solvent for GH and it is possible that it can disturb the formation of dentine Earlier investigators (Branemark & Goldie 1967 Branemark Goldie & Lindstrom 1967) have found deleterious effects of the suspension medium for a corticosteroid preparation when locally applied to experimental animals The effect was found attributable to sorbitol

At present the finding can only be noted no definite explanation can be offered and further investigations are desirable Anyhow the difference between animals given suspension medium and those given cortisol was so great that no doubt should exist that cortisol itself in the dosage employed has a profoundly retarding effect on the rate of incisor dentine apposition

The present investigation has not shown how the hormones exert their effects A very complicated chain of events may be at work The effects found are connected with the administration of the hormones Similar effects were obtained by administration of the solvent respectively the suspension medium but the effect of the hormones were highly significantly different from that of the suspension medium or the solvent alone

constituents of the solvent. It is possible that the handling of the animals every day during the experimental period is the cause. It has been claimed that the more rats are handled the tamer and quieter they become and then probably grow more quickly (Lane Petter 1963). This assumption may be supported by the fact that the effect of solvent was only seen in young animals which can be expected to be more sensitive than adults. It has been claimed that children subjected to stress grow taller and it seems certain that stimulation of rats during *infancy may cause increase in the rate of growth (Whiting, Landauer* & Jones 1968).

With the method developed measurements can be performed with high precision. This fact and the possibility that the test system is easily influenced by various factors, especially in young animals, may explain the unexpected finding.

It is not easy definitely to decide whether GH has an effect or not. Even if highly significant differences were found, the absolute differences between the values measured were not so large (Tables *XXXII—XXXIV, XL—XLII). However, and this may be the important* finding, in all of the 3 categories of animals treated with GH, adult animals both primary and control experiments, and young animals, the results of GH treatment point in the same direction and indicate that GH has an accelerating effect on upper incisor dentine formation in the intact female white rat. The conclusion may be drawn that it is highly probable that a true and not an apparent effect was found. The results are in conformity with those obtained by earlier investigators who used longer experimental periods and less precise methods.

Hydrocortisone

A retarding effect was demonstrable already in the histologic sections (Fig. 49, page 84). Also the values measured (Tables XLVIII—L) clearly demonstrated that a decrease occurred and the final proof was produced by the statistical analysis which showed a highly significant decrease during cortisol treatment. Young odontoblasts seem to be less responsive than older ones (Figs. 50—51, pages 87—88).

Again the vehicle was found to have an effect in the same direction as the hormone. In the interpretation of the fact that the decrease compared with that in normal animals was significant but not highly significant, it should be borne in mind *that no difference was found be*tween the effect of suspension medium for cortisol and that of the sol

RESULTS AND DISCUSSION

In the specimens from untreated animals neither on the endosteal nor on the periosteal side was bone formation present on the whole circumference of the bone at the same time. Parts of the circumference showed bone formation and at these places fluorescent bands were visible (Fig. 52).

A possible source of error should be mentioned. Though only 5 injections of OTC have been given 6 fluorescent bands were visible. This can be explained by the observation that during the grinding of sections OTC is dissolved from the bone and is present in the water during grinding and is absorbed to the surface of bone. The same finding can be made in dentine. If a section from a tooth from an animal given no injections of OTC is ground with the aid of equipment previously used for the grinding of sections from animals given OTC a fluorescent band will be found in the boundary between dentine and the pulp chamber. If a section from an animal given no injections of OTC is ground with



Fig. 5 Transverse section from tibia 4 month old normal rat. On endosteal side 5 fluorescent bands (6 days interval). What appears as the 6th band is an artefact. 3 ×

VII

TENTATIVE COMPARISON BETWEEN APPOSITION OF INCISOR DENTINE AND LAMELLAR BONE

INTRODUCTION

Garn, Lewis & Blizzard (1965) compared dental and skeletal development in some endocrine disturbances in man. They found that the retardation or acceleration of development was less pronounced in *dental than in skeletal tissues, in dental tissues only half as much or* one fourth of that in skeletal tissues. In congenital adrenal hyperplasia Bergstrand & Filipsson (1967) preliminarily reported a similar finding: *dental development was less advanced than skeletal development*.

In the present investigation an attempt was made to compare the formation of dentine and of lamellar bone.

MATERIAL AND METHODS

As mentioned above, the femur and the tibia on each side had been extracted and stored in the cold. For the investigation the right femur and tibia were selected from the following experimental categories: 5 month old normal adult animals, 4 month old animals given GH or cortisol (primary experiments) and the 4 month old adult animals used for control experiments. Only those animals where the investigation of the dentine had shown no missing fluorescent bands were used.

From the middle third of the unembedded femur and the tibia 3 transverse sections were taken from each bone and ground according to the method described by Frost (1958). After passing through absolute alcohol and xylol they were mounted in DePeX. All together 411 histologic sections, 127 from untreated, 75 from GH treated and 209 from cortisol treated animals were investigated.

RESULTS AND DISCUSSION

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Fig 53 Transverse section from tibia 4 month old normal rat On endosteal side 5 fluorescent bands (6 days interval) What appears as the 6th band is an artefact 3 ×

the aid of completely fresh equipment no fluorescent band will be found

It was very soon realised that good quantitative measurement of the rate of lamellar bone formation could not be made This was because the fluorescent bands did not regularly occur round the whole periphery of the bone with the result that it was not possible to make measurements at corresponding parts of the sections from different animals It is theoretically possible to overcome this difficulty by *making comparisons between untreated and treated periods in the* same section at randomly selected points where bone formation occurred during the whole experimental period But in practice this seemed inconvenient because even if a point was selected and measurements were made along the corresponding radius the rate of apposition during *periods of equal length varied widely even in normal animals Also the* variation between different points on the circumference was considerable It may be possible to make a very great number of measurements in untreated and for example hormone treated animals and then com

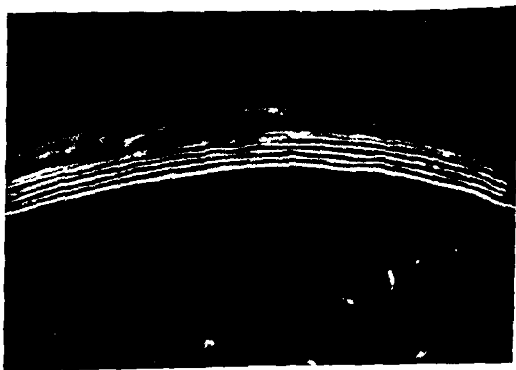


Fig 53 Transverse section from femur 4 month old normal rat Periosteal side Five fluorescent bands visible (6 days interval) 14×

pare the quotients between periods of treatment and no treatment but it is very doubtful whether such comparisons would be really informative

Sections were nevertheless made from bones from the animals in the primary experiments and examined in the hope that it would reveal substantial differences if any between periods of treatment and no treatment It was found that normal and GH treated animals behaved alike and no certain difference could be detected between them

In animals given cortisol at most 3 fluorescent bands could be detected *In every one of the untreated and of the GH treated animals* 5 bands could always be seen in at least one histologic section from every animal For purposes of control 3 sections were also taken from the femur and the tibia on the left side of cortisol treated animals (primary experiments) and here too at most 3 fluorescent bands were seen

The findings were the same in the animals in the control experiments Normal and GH treated animals behaved alike Five fluorescent bands were found in at least one histologic section from each animal *i e*

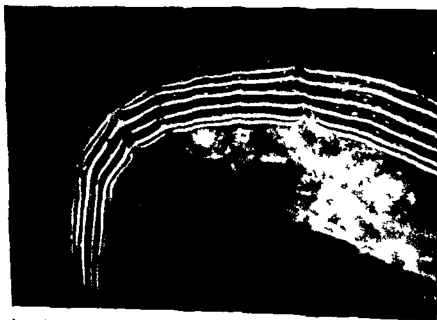


Fig 54 Transverse section from tibia 4 month old normal rat Endosteal side Five fluorescent bands visible (6 days interval) (6th band artefact) 14 ×

the aid of completely fresh equipment no fluorescent band will be found

It was very soon realised that good quantitative measurement of the rate of lamellar bone formation could not be made This was because the fluorescent bands did not regularly occur round the whole periphery of the bone with the result that it was not possible to make measurements at corresponding parts of the sections from different animals It is theoretically possible to overcome this difficulty by making comparisons between untreated and treated periods in the same section at randomly selected points where bone formation occurred during the whole experimental period But in practice this seemed inconvenient because even if a point was selected and measurements were made along the corresponding radius the rate of apposition during periods of equal length varied widely even in normal animals Also the variation between different points on the circumference was considerable It may be possible to make a very great number of measurements in untreated and for example hormone treated animals and then com

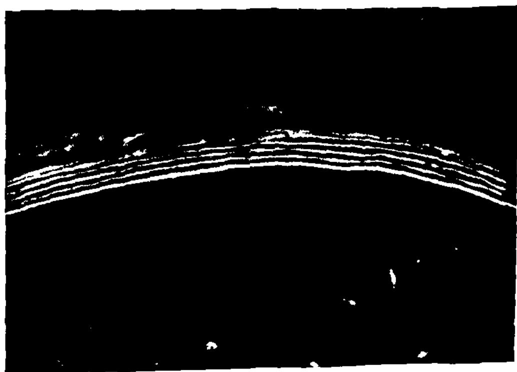


Fig 53 Transverse section from femur 4 month old normal rat Periosteal side Five fluorescent bands visible (6 days interval) 14

during the preparation of sections This explanation may perhaps hold for the bone formed on the periosteal side but seems less likely for that on the endosteal side where the last formed bone appears to be more protected The findings in cortisol treated animals were the same on both the periosteal and endosteal side To rule out this possible source of error some sections from the left side of animals used in the con trol experiments were embedded in Ward s Bioplastic and then ground but the finding was the same as in unembedded sections

The results may be *summarised* as follows *It is not possible to mea* sure the rate of peri and endosteal bone apposition in the femur and the tibia in adult rats accurately by performing linear measurements between the fluorescent bands The short term administration of GH has no certain effect Administration of very large doses of cortisol seems to result in complete arrest of lamellar bone formation This last finding parallels the simultaneous retardation of incisor dentine for mation

Concerning this parallelism in mode of reaction it may be mentioned that the rate of longitudinal growth from the proximal growth plate of tibia has been studied in normal solvent treated and GH treated young animals used in the present investigation GH was *found to accelerate* this growth highly significantly (Ahlgren & Hansson unpublished observations)

bone formation occurred during the whole experimental period (Figs 53—54) In the animals given cortisol at most 3 bands could be detected on the endosteal and periosteal sides (Fig 55) Animals given solvent for GH or suspension medium for cortisol exhibited the same features as the untreated and the GH treated animals

The result indicated that during the treatment with cortisol no formation of bone occurred or was so low that the chronologically last 3 fluorescent bands could not be separated However the last band was not so thick that it could be suspected of consisting of 3 confluent bands (Fig 55) It is also remotely possible that the bands seen were not the ones resulting from the first 3 injections of OTC but from the last injections In view of the findings in untreated animals this explanation was considered improbable The most probable explanation is that during treatment with cortisol in very large doses lamellar bone formation completely stops

One might imagine that during cortisol treatment bone is formed but its mineralisation is so defective that it is very soft and is lost

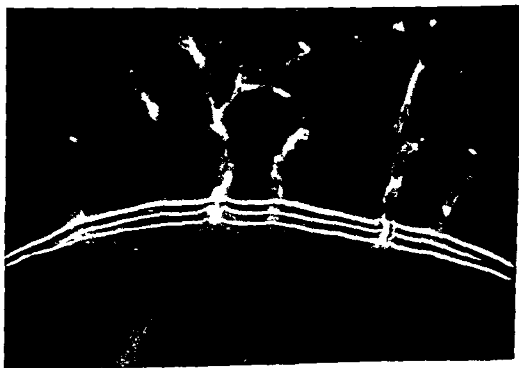


Fig 55 Transverse section from femur Endosteal side 4 month old rat treated with hydrocortisone Only 3 fluorescent bands visible (6 days interval) 14

is suggested that different types of growth can be described with S shaped curves

Administration of pituitary growth hormone in excess produced a slight but highly significant increase in the rate of apposition of dentine as investigated in adult and young intact female rats

Administration of hydrocortisone in excess produced a highly significant decrease in the rate of dentine apposition as investigated in adult female rats Young cells tended to be less sensitive

In an attempt to compare the rate of formation of dentine with that of lamellar bone in adult female rats it was found that the use of oxytetracycline as a marking agent would not allow precise quantitative determination of the linear rate of formation of periosteal and endosteal lamellar bone A direct numerical comparison between the rate of formation of dentine and of lamellar bone was therefore not possible Both types of tissue were susceptible to hydrocortisone which suppressed the rate of formation of dentine and caused apparently complete cessation of formation of lamellar bone

SUMMARY

In the course of personal preliminary studies of bone healing and lamellar bone formation under the influence of the growth hormone it was thought that dentine might serve as a test tissue for investigations of hormonal influence. The chemical and submicroscopic structure of dentine is similar to that of bone and in normal dentine no resorption occurs.

According to the literature, rat incisor dentine normally forms at a constant rate and is very sensitive to influences. Personal preliminary investigations failed to wholly confirm this view. A re-investigation was considered necessary.

Using oxytetracycline as a marking agent a technique was devised for measuring the linear rate of apposition of dentine in different parts of the upper incisors from the apex to the incisal edge and from different places on the circumference. Statistical analysis of the values measured (mostly with the aid of computer) was performed. The rate of incisor dentine apposition varied in a regular but more complicated manner than earlier known. From the apex to the incisal edge of the incisor 3 phases could be recognised: a rising one, a maximum one and a falling one. Studies on female rats of different ages revealed the same general pattern but in young animals the course of events was faster. Based on the results of the computer analysis a technically simpler but not less informative statistical analysis was devised. The "functional age" of the odontoblasts could be related to the rate of apposition of dentine. Young and old cells produced less dentine per unit of time than did those of intermediate age.

The apposition of dentine is briefly compared with other types of growth and with the rate of bone formation in a Haversian system. It

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APPENDIX

Tables I—II Analysis of covariance 5 month old normal rats

Table I

Source of variation	Set 3—4 Right m sq	d f	Left m sq	d f	4—5 Right m sq	d f	Left m sq	d f	Right and Left m sq	d f
T	36.1	9	36.3	8	14.2	6	1.9	6	9.6	10
S	1811.[illegible]	3	1135.5	3	5[illegible]7.6	4	574.5	4	908.1	4
P	35[illegible].9	9	3[illegible]6.1	9	[illegible]3.[illegible]	9	73.0	9	115.3	9
TS	[illegible]3.[illegible]	2[illegible]	27.0	[illegible]4	4.4	24	4.8	24	4.7	40
TP	3.[illegible]	81	2.5	7[illegible]	1.5	54	1.0	54	1.3	90
SP	51.1	[illegible]	45.6	2	1[illegible].9	36	14.8	36	20.9	36
TSP	[illegible].8	243	[illegible].3	216	1.3	216	1.0	216	1.2	360
R	0.6	3[illegible]9	0.6	359	0.5	319	0.4	349	0.4	549

Table II

Source of variation	Set 3 Right m sq	d f	Left m sq	d f	4 Right m sq	d f	Left m sq	d f	5 Right m sq	d f	Left m sq	d f
T	16	6	10.4	9	24.[illegible]	13	43.4	12	28.6	11	64.5	9
I	53[illegible].5	3	6[illegible] 6	3	603.0	3	334	3	6301.6	3	4 486	3
I	409.0	[illegible]	503.8	9	508.8	9	496.9	9	31[illegible].5	9	[illegible]86.2	9
TI	8.4	18	12.4	7	38.0	39	41.9	3[illegible]	16.5	33	[illegible]6.[illegible]	2
TI	3.5	54	6.0	81	7.2	117	6.3	108	6.6	99	5.4	81
IP	[illegible]0.0	2	[illegible]5.5	2	46.3	[illegible]	45.0	[illegible]7	6[illegible].3	[illegible]7	61.8	2[illegible]
TIP	[illegible].8	1[illegible]	2.5	[illegible]43	3.9	351	3.3	3[illegible]4	3.3	29	3.6	243
R	1.0	[illegible]9	1.2	3[illegible]9	1.5	5[illegible]9	1.2	519	1.5	4[illegible]9	1.2	399

Table III *Calculated values for dentine apposition for 10 measuring points taken together 5 month old normal rats Figures in brackets denote number of animals*

Set 3—4 Right	Left	4—5 Right	Left	3 Right	Left	4 Right	Left	5 Right	Left
—		6.5	6.3	14.1	14	1[illegible].2	1[illegible].7	19.5	19.[illegible]
13.7	14.1	9.0	8.9	16.6	16.3	18.4	18.0	1[illegible].[illegible]	17.6
1[illegible].9 (10)	1[illegible].6 (9)	9.4	9.4	18.1	1[illegible].[illegible] (10)	17.6 (12)	17.6 (12)	13.3 (12)	13.8 (10)
1[illegible].0	1[illegible].0		7.8	18.4	18.2	14.8	1[illegible].5	[illegible]	8.0
11.1	1[illegible].4	4.0	4.1		—	—	—	—	—

Table IV *Standard deviations of values in Table III*

Set 3—4 Right	Left	4—5 Right	Left	3 Right	Left	4 Right	Left	5 Right	Left
1.0	1.0	0.6	0.6	1.2	1.0	0.9	0.9	0.9	1.0

Tables I—II *Analysis of covariance 5 month old normal rats*

Table I

Source of variation	Set 3—4 Right m sq	d f	Left m sq	d f	4—5 Right m sq	d f	Left m sq	d f	Right and Left m sq	d f
T	30 1	9	36 3	8	14 2	6	1 9	6	9 6	10
S	1811 2	3	1135.5	3	5476	4	5745	4	9031	4
P	3529	9	3 61	9	3 7	9	730	9	115.3	9
TS	23	2	2.0	24	4 4	24	4.8	24	4 7	40
TI	3 6	81	2 5	2	1.5	54	1 0	54	1 3	90
SP	51 1	27	45 6	27	12 9	36	14 8	36	20 9	36
TSP	2 8	243	2 3	216	1 3	216	1 0	216	1 2	360
R	0 6	339	0 6	359	0 5	349	0 4	349	0 4	549

Table II

Source of Variation	Set 3 Right m sq	d f	Left m sq	d f	4 Right m sq	d f	Left m sq	d f	5 Right m sq	d f	Left m sq	d f
T	16 7	6	10 4	9	24 2	13	43 4	12	28 6	11	64 5	9
I	536 5	3	69 6	3	6030	3	3317	3	6301 6	3	4486	3
P	4080	9	5038	9	5088	9	4969	9	3125	9	286.2	9
TI	8 4	18	12 4	2	38 0	39	41 9	36	16.5	33	26 2	2
TI	3.5	54	6 0	81	[illegible]	11	6 3	108	6 6	99	5 4	81
IP	0 0	27	2 5	27	40 3	27	45 0	7	64 3	27	61 8	27
TII	2 8	162	2 5	243	3 9	3 1	3.3	3 4	3 9	297	3 6	243
R	1 0	2 9	1 2	339	1 5	559	1 2	519	1 5	4 9	1 2	309

Table III *Calculated values for dentine apposition for 10 measuring points taken together 5 month old normal rats Figures in brackets denote number of animals*

Set 3—4 Right	Left	4—5 Right	Left	3 Right	Left	4 Right	Left	5 Right	Left
	—	6	6 3	14 1	14	17 2	16 7	19	19 2
13 7	14 1	9 0	8 9	16 6	16 3	18 4	18 0	17 2	17 6
1 9 (10)	1 6 (9)	3 4	9 4	18 1	17 6 (10)	1 6 (12)	17 6 (12)	13 3 (12)	13 8 (10)
1 0	17 0	7 7	8	18 4	18 2	14 8	15 5	7	8 0
11 1	12 4	4 0	4 1	—	—	—	—	—	—

Table IV *Standard deviations of values in Table III*

Set 3—4 Right	Left	4—5 Right	Left	3 Right	Left	4 Right	Left	5 Right	Left
1 0	1 0	0 6	0 6	1 2	1 0	0 9	0 9	0 9	1 0

Tables I—II *Analysis of covariance 5 month old normal rats*

Table I

Source of variation	Set 3—4 Right m sq	d f	Left m sq	d f	4—5 Right m sq	d f	Left m sq	d f	Right and Left m sq	d f
T	36.1	9	36.3	8	14.2	6	1.9	6	9.6	10
S	1811.[illegible]	3	1135.5	3	577.6	4	571.5	4	908.1	4
I	3[illegible]9	9	3 6 1	9	[illegible]37	[illegible]	[illegible]30	9	115.3	9
TS	[illegible]3.7	[illegible]	[illegible]7.0	24	4.4	[illegible]4	1.8	24	4.[illegible]	40
TI	3.6	81	2.5	[illegible]	1.5	54	1.0	54	1.3	[illegible]0
SI	51.1	27	45.6	27	1[illegible].9	36	14.8	36	20.9	36
TSP	[illegible].8	243	[illegible].3	216	1.3	216	1.0	216	1.[illegible]	360
R	0.[illegible]	3[illegible]	0.6	359	0.5	349	0.4	349	0.4	549

Table II

Source of variation	Set 3 Right m sq	d f	Left m sq	d f	4 Right m sq	d f	Left m sq	d f	5 Right m sq	d f	Left m sq	d f
T	16.[illegible]	6	10.4	9	[illegible]4.[illegible]	13	43.4	1[illegible]	29.[illegible]	11	61.5	9
I	530.5	3	6[illegible]6.6	3	603.0	3	334.7	3	6301.6	3	4,486	3
I	408.0	[illegible]	503.8	9	508.8	9	496.9	9	312.5	9	286.2	9
TI	8.4	18	12.4	27	38.0	30	41.9	6	16.5	33	[illegible]6.2	[illegible]7
TI	3.5	54	6.0	81	2	117	6.3	108	6.6	99	5.4	81
II	[illegible]0.0	27	5.5	[illegible]	40.3	[illegible]7	45.0	[illegible]7	6 3	27	61.8	27
TII	2.8	16	[illegible].5	[illegible]43	[illegible].9	351	3.3	3[illegible]4	3.9	29	3.[illegible]	243
R	1.0	[illegible]9	1.[illegible]	309	1.[illegible]	559	1.[illegible]	519	1.5	4[illegible]0	1.[illegible]	309

Table III *Calculated values for dentine apposition for 10 measuring points taken together 5 month old normal rats Figures in brackets denote number of animals*

Set 3—4 Right	Left	4—5 Right	Left	3 Right	Left	4 Right	Left	5 Right	Left
		6.5	6.3	14.1	14	17.2	1[illegible].7	19	19.[illegible]
13.7	14.1	[illegible].0	8.9	1[illegible].6	16.3	18.4	18.0	1[illegible].[illegible]	17.6
1[illegible].9 (10)	1[illegible].6 (9)	[illegible].4	9.4	18.1 ([illegible])	17.6 (10)	1[illegible].6 (1[illegible])	1[illegible].6 (12)	13.3 (12)	13.8 (10)
1[illegible].0	1[illegible].0		7.8	19.4	18.2	14.8	15.5	7.[illegible]	8.0
11.1	12.4	4.0	4.1		—	—	—	—	—

Table IV *Standard deviations of values in Table III*

Set 3—4 Right	Left	4—5 Right	Left	3 Right	Left	4 Right	Left	5 Right	Left
1.0	1.0	0.6	0.6	1.2	1.0	0.9	0.9	0.9	1.0

Tables I—II Analysis of covariance 5 month old normal rats

Table I

Source of variation	Set 3—4 Right m sq	d f	Left m sq	d f	4—5 Right m sq	d f	Left m sq	d f	Right and Left m sq	d f
T	36 1	9	36 3	8	14 ?	6	1 9	6	9 ?	10
S	1811 ?	3	1135.5	3	5?7 6	4	574.5	4	908 1	4
I	35?9	9	3 6 1	9	3 ?	9	3 0	9	115 3	9
TS	?3 7	27	?7 0	?4	4 4	?4	4 8	24	4	40
TI	3 ?	81	?5	??	1.5	54	1 0	54	1 3	90
SI	51 1	2	45 6	??	12 9	36	14.8	36	20 9	36
TSP	?.8	?43	?.3	216	1.3	?16	1 0	216	1 ?	360
R	0 6	399	0 6	35?	0 5	34?	0 4	319	0 4	549

Table II

Source of variation	Set 3 Right m sq	d f	Left m sq	d f	4 Right m sq	d f	Left m sq	d f	5 Right m sq	d f	Left m sq	d f
T	16	6	10 4	9	24 2	13	43 4	12	?8 ?	11	64 5	9
I	53C 5	3	6? 6	3	603 0	3	331 7	3	6301 6	3	4,48 6	3
I	408 0	9	03 8	9	508 8	9	40? 9	9	31 5	9	?86.2	9
TI	8 4	18	1? 4	27	38 0	39	41 ?	36	1?.5	33	?6 ?	2
TI	3 5	54	6 0	81	7 ?	117	6 3	108	? 6	99	5 4	81
IP	?0 0	27	?5 5	27	4? 3	?7	45 0	??	6 3	27	61 8	27
TII	? 8	16?	? 5	?43	3 9	3 1	3.3	3?4	3 9	29?	3 6	243
R	1 0	? 9	1 2	399	1.5	559	1 ?	1?	1 5	4 9	1 ?	399

Table III Calculated values for dentine apposition for 10 measuring points taken together 5 month old normal rats Figures in brackets denote number of animals

Set 3 4 Right	Left	4 5 Right	Left	3 Right	Left	4 Right	Left	5 Right	Left
		6	6 3	11 1	11 ?	1? 2	1C ?	19 5	19 ?
13	14 1	5 0	8 9	16 6	16 3	19 4	18 0	17 ?	1? 6
1 9 (10)	1 6 (9)	5 4	9 4	19 1	1 ? (10)	1 6 (1?)	17 6 (12)	13 ? (12)	13 8 (10)
1 0	1 0		8	19 4	18 2	14 9	15 5		8 0
11 1	12 4	4 0	4 1		—	—	—	—	—

Table IV Standard deviations of values in Table III

Set 3 4 Right	Left	4—5 Right	Left	3 Right	Left	4 Right	Left	5 Right	Left
1 0	1 0	0 6	0 6	1 2	1 0	0 9	0 9	0 9	1 0

Tables I—II *Analysis of covariance 5 month old normal rats*

Table I

Source of variation	Set 3—4 Right m sq	d f	Left m sq	d f	4—5 Right m sq	d f	Left m sq	d f	Right and Left m sq	d f
T	36 1	9	36.3	8	14 2	6	1 9	6	9 6	10
S	1811 2	3	1135 5	3	577 6	4	574 5	4	908 1	4
P	3529	9	3 6 1	[illegible]	3 7	9	3 0	9	115 3	9
TS	23	[illegible]	27 0	24	4 4	24	4.8	24	4 7	40
TP	3 6	81	2 5	2	1.5	54	1 0	54	1.3	90
SP	51 1	[illegible]	45 6	[illegible]	12 9	36	14.8	36	20 9	36
TSP	2 8	243	2 3	216	1.3	216	1 0	216	1 2	360
R	0 6	309	0 6	309	0.5	349	0 4	349	0 4	549

Table II

Source of variation	Set 3 Right m sq	d f	Left m sq	d f	4 Right m sq	d f	Left m sq	d f	5 Right m sq	d f	Left m sq	d f
T	16 7	6	10 4	9	21 2	13	43 4	12	28 6	11	64 5	9
I	536.5	3	627 6	3	603 0	3	334 7	3	6301 6	3	4 48 6	3
I	408 0	9	503.8	9	508 8	9	496 9	9	312 5	9	236.2	9
TI	8 4	18	12 4	27	38 0	39	41 9	36	16 5	33	26	27
TI	3.5	54	6 0	81	7 2	117	6.3	108	6 6	99	5 4	81
II	0 0	27	[illegible]	27	46.3	27	45 0	27	6 3	27	61 8	27
TII	2 8	[illegible]	2.5	243	3 9	[illegible]	3.3	324	3 9	297	3 6	243
R	1 0	2 9	1 2	309	1 5	509	1.2	519	1.5	4 9	1.2	309

Table III *Calculated values for dentine apposition for 10 measuring points taken together 5 month old normal rats Figures in brackets denote number of animals*

Set 3 4 Right	Left	4 5 Right	Left	3 Right	Left	4 Right	Left	5 Right	Left
		6 5	6 3	14 1	14	1 2	16 7	19	19 2
13 7	14 1	9 0	8 9	16 6	16 3	18 4	18 0	1 [illegible]	1 6
1 9 (10)	1 6 (9)	9 4	9 4	18 1	17 [illegible] (10)	1 6 ([illegible])	1 6 (12)	13 3 (12)	13 8 (10)
1 0	1 0		8	19 4	18 2	14 8	1 5	[illegible]	8 0
11 1	12 4	4 0	4 1		—	—	—	—	—

Table IV *Standard deviations of values in Table III*

Set 3 4 Right	Left	4—5 Right	Left	3 Right	Left	4 Right	Left	5 Right	Left
1 0	1 0	0 6	0 6	1 2	1 0	0 9	0 9	0 9	1 0

Table V *Calculated values for dentine apposition at each of the 10 points in each of the sets Right side 5 month old normal rats Figures in brackets denote number of animals Cf Table XXV*

Measuring point	1	2	3	4	5	6	7	8	9	10
Set 3—4	19 2	15 3	19 0	14 8	11 7	12 8	12 8	11 8	9 7	12 6
	22 1	18 4	21 0	19 0	16 5	11 7	17 5	14 2	15 7	18 9
	19 2 (18)	18 3 (18)	18 8 (17)	18 4 (17)	16 4 (16)	17 3 (16)	17 7 (12)	17 0 (11)	16 0 (16)	18 0 (17)
	10 8	15 2	12 4	12 8	11 3	8 6	13 4	8 3	10 6	9 7
Set 4—5	9 7	7 3	8 4	6 7	5 2	5 9	5 5	5 3	1 5	5 9
	11 1	8 9	10 9	9 6	7 9	7 5	8 6	7 3	7 7	9 2
	10 5 (11)	9 1 (12)	11 1 (11)	10 1 (12)	9 5 (12)	7 5 (13)	9 6 (11)	7 6 (11)	8 6 (11)	9 9 (11)
	7 8	8 0	9 0	8 3	7 2	6 0	8 6	6 2	7 1	7 8
	3 0	5 6	4 6	4 1	3 8	3 0	5 5	3 0	3 2	3 0
Set 3	19 3	14 8	17 3	13 6	11 2	12 0	12 4	12 6	10 2	13 0
	21 2	16 7	20 2	17 3	14 9	15 0	15 2	14 4	12 5 (11)	15 3
	22 4 (14)	17 0 (15)	21 7 (14)	19 4 (14)	16 8 (12)	15 9 (11)	17 5 (8)	15 0 (7)	15 2	17 9 (12)
	22 7	18 4	21 8	20 0	17 2	14 6	19 3	14 4	18 6	21 1
Set 4	21 3	17 3	21 5	18 4	15 4	15 7	15 6	15 3	13 5	16 2
	22 5	18 8	21 4	19 9	17 3	15 2	17 6	14 9	16 7	19 5
	20 4 (16)	19 8 (16)	20 2 (16)	19 4 (15)	16 9 (15)	11 0 (15)	18 4 (14)	13 6 (15)	17 0 (15)	19 2 (15)
	11 9	17 3	17 9	16 9	11 3	12 2	18 1	11 4	14 6	15 4
Set 5	23 9	18 9	22 4	21 5	18 6	10 4	18 8	16 3	17 7	21 0
	19 2	18 5	18 9	18 4	16 3	13 3	17 5	13 5	10 0	18 4
	13 1 (14)	15 9 (16)	14 4 (14)	14 0 (15)	12 4 (14)	10 0 (15)	15 1 (15)	10 2 (15)	12 2 (15)	13 0 (15)
	5 6	11 3	8 9	8 2	7 1	6 [illegible]	11 6	6 2	6 4	1 [illegible]

Table VI *Standard deviations of values in Table V*

Measuring point	1	2	3	4	5	6	7	8	9	10
Set										
3—4	0 [illegible]	0 3	0.5	0 5	0 5	0 4	0	0 4	0 4	0 6
4—5	0 5	0 3	0 4	0 4	0.3	0 3	0 3	0.3	0.3	0.5
3	0 [illegible]	0.3	0.5	0 5	0 5	0 5	0 [illegible]	0 [illegible]	0 4	0 5
4	0 [illegible]	0 3	0.5	0.5	0 5	0 [illegible]	0 [illegible]	0 5	0 5	0.8
5	0 [illegible]	0 4	0 7	0 6	0 [illegible]	0 4	0 [illegible]	0 5	0 [illegible]	0 7

Table VII *Means of measured values for dentine apposition at point 2 for interval 3 (8 days) in groups of 5 classes 5 month old normal rats*

Midpoint of groups of classes	Number of observations (n)	Mean	SD
3	[illegible]	13.[illegible]	
8	10	14 6	
13	19	15 1	
18	16	15	
23	11	17.[illegible]	
[illegible]	1[illegible]	17	0.8 √n
33	13	18.[illegible]	
38	10	18.[illegible]	
43	10	18 [illegible]	
48	10	19.[illegible]	
53	11	18 3	
58	11	1[illegible].5	
[illegible]3	11	16 4	
68	9	1[illegible] 0	1.8 √n
3	5	14 6	
	Total 183		

Table V *Calculated values for dentine apposition at each of the 10 points in each of the sets Right side 5 month old normal rats Figures in brackets denote number of animals Cf Table XXV*

Measuring point	1	2	3	4	5	6	7	8	9	10
Set 3—4	19 2	15 3	19 0	14 8	11 7	12 8	12 8	11 8	9 7	12 6
	22 1	18 4	21 0	19 0	16 5	14 7	17 5	14 2	15 7	18 9
	19 2 (18)	18 3 (18)	18 8 (17)	18 4 (17)	16 4 (16)	13 3 (16)	17 7 (12)	13 0 (14)	16 0 (16)	18 0 (17)
	10 8	1[illegible] 2	12 4	12 8	11 3	8 6	13 4	8 3	10 6	9 7
Set 4—5	9 7	7 3	8 4	6 7	5 2	5 9	5 5	5 3	4 5	5 9
	11 1	8 9	10 9	9 6	7 9	7 5	8 6	7 3	7 7	9 2
	10 5 (11)	9 1 (12)	11 1 (11)	10 1 (12)	8 [illegible] (12)	7 5 (13)	9 6 (11)	7 6 (11)	8 6 (11)	9 9 (11)
	7 8	8 0	9 0	8 3	7 2	6 0	8 6	6 2	7 1	7 8
	3 0	5 6	4 6	4 1	3 8	3 0	5 5	3 0	3 2	3 0
Set 3	19 3	11 8	17 3	13 6	11 2	12 0	12 4	12 6	10 2	13 0
	21 2	16 7	20 2	17 3	14 9	15 0	15 2	11 4	12 5	15 3
	22 1 (14)	17 9 (15)	21 7 (14)	19 4 (14)	16 8 (12)	15 9 (11)	17 [illegible] (8)	15 0 (7)	15 2 (11)	17 9 (12)
	22 7	18 4	21 8	20 0	17 2	14 6	19 3	14 4	18 6	21 1
Set 4	21 3	17 3	21 5	18 4	15 4	15 7	15 6	15 3	13 5	16 2
	22 [illegible]	18 8	21 4	19 9	17 3	1[illegible] 2	17 0	14 9	16 7	19 5
	20 4 (16)	18 8 (16)	20 2 (16)	19 4 (15)	16 9 (15)	14 0 (1[illegible])	18 4 (14)	13 6 (1[illegible])	17 0 (15)	19 2 (15)
	14 9	17 3	17 8	16 9	14 3	12 2	18 1	11 4	14 6	1[illegible] 4
Set 5	23 9	18 9	22 4	21 [illegible]	18 6	10 4	18 8	16 3	17 7	[illegible]1 0
	19 [illegible]	18 [illegible]	18 9	18 4	16 3	13 3	17 5	13 [illegible]	16 0	18 4
	13 1 (14)	1[illegible] 9 (16)	14 4 (14)	14 0 (1[illegible])	12 4 (14)	10 0 (1[illegible])	15 1 (1[illegible])	10 2 (15)	12 2 (15)	13 0 (15)
	5 0	11 3	8 9	8 2	7 1	6 [illegible]	11 6	6 2	6 4	1 9

Table VI *Standard deviations of values in Table V*

Measuring point	1	2	3	4	5	6		8	9	10
Set										
3–4	0.6	0.3	0.5	0.5	0.5	0.4	0.5	0.4	0.4	0.6
4–5	0.5	0.3	0.4	0.4	0.3	0.3	0.3	0.3	0.3	0.5
3	0.6	0.3	0.5	0.5	0	0.5	0.7	0.6	0.4	0.5
4	0.7	0.3	0.5	0.5	0.5	0.6	0.5	0.5	0	0.8
5	0.[illegible]	0.4	0.7	0.6	0.6	0.4	0.6	0.5	0.6	0.7

Table VII *Means of measured values for dentine apposition at point 2 for interval 3 (8 days) in groups of 5 classes 5 month old normal rats*

Midpoint of groups of classes	Number of observations (n)	Mean	SD
3	20	13	
8	10	14.6	
13	19	15.1	
18	16	15.7	
23	11	17.5	
28	[illegible]	[illegible]	0.8 √n
33	13	18.5	
38	10	18.5	
43	10	19.6	
48	10	18.5	
53	11	18.3	
58	11	[illegible]	
63	11	16.4	
68	9	16.0	1.8 √n
73	5	14.6	
	Total 183		

Table V Calculated values for dentine apposition at each of the 10 points in each of the sets Right side 5 month old normal rats Figures in brackets denote number of animals Cf Table XXV

Measuring point	1	2	3	4	5	6	7	8	9	10
Set 3—4	19 2	15 3	19 0	14 8	11 7	12 8	12 8	11 8	9 7	12 6
	22 1	18 4	21 0	19 0	16 5	14 7	17 5	14 2	15 7	18 9
	19 2 (18)	18 3 (18)	18 8 (17)	18 4 (17)	16 4 (16)	13 3 (16)	17 7 (12)	13 0 (14)	16 0 (16)	18 0 (17)
	10 8	15 2	12 4	12 8	11 3	8 6	13 4	8 3	10 6	9 7
Set 4—5	9 7	7 3	8 4	6 7	5 2	5 9	5 5	5 3	4 5	5 9
	11 1	8 9	10 9	9 6	7 9	7 5	8 6	7 3	7 7	9 2
	10 5 (11)	9 1 (12)	11 1 (11)	10 1 (12)	8 5 (12)	7 5 (13)	9 6 (11)	7 6 (11)	8 6 (11)	9 9 (11)
	7 8	8 0	9 0	8 3	7 2	6 0	8 6	6 2	7 1	7 8
	3 0	5 6	4 6	4 1	3 8	3 0	5 5	3 0	3 2	3 0
Set 3	19 3	14 8	17 3	13 6	11 2	12 0	12 4	12 6	10 2	13 0
	21 2	16 7	20 2	17 3	14 9	15 0	15 2	14 4	12 5	15 3
	22 4 (14)	17 9 (15)	21 7 (14)	19 4 (14)	16 8 (12)	15 9 (11)	17 5 (8)	15 0 (7)	15 2 (11)	17 9 (12)
	22 7	18 4	21 8	20 0	17 2	14 6	19 3	14 4	18 6	21 1
Set 4	21 3	17 3	21 5	18 4	15 4	15 7	15 6	15 3	13 5	16 2
	22 [illegible]	18 8	21 4	19 9	17 3	15 2	17 6	14 9	16 7	19 [illegible]
	20 4 (16)	18 8 (16)	20 2 (16)	19 4 (15)	16 9 (15)	14 0 (15)	18 4 (14)	13 6 (15)	17 0 (1[illegible])	19 2 (15)
	11 9	17 3	17 8	16 9	14 3	12 2	18 1	11 4	14 6	15 4
Set 5	23 9	18 9	22 4	21 [illegible]	18 6	16 4	18 8	16 3	17 7	[illegible]1 0
	19 2	18 [illegible]	18 9	18 4	16 3	13 3	17 5	13 5	16 0	18 4
	13 1 (14)	15 9 (16)	14 4 (14)	14 0 (1[illegible])	12 4 (14)	10 0 (1[illegible])	15 1 (1[illegible])	10 2 (1[illegible])	12 2 (15)	13 0 (1[illegible])
	[illegible]6	11 3	8 9	8 2	7 1	6 5	11 6	6 2	[illegible]4	4 9

Table VI Standard deviations of values in Table V

Measuring point	1	2	3	4	5	6	7	8	9	10
Set										
3–4	0.6	0.3	0.5	0.5	0.5	0.4	0.5	0.4	0.4	0.6
4–5	0.5	0.3	0.4	0.4	0.3	0.3	0.3	0.3	0.3	0.5
3	0.6	0.3	0.5	0.5	0.5	0.5	0.7	0.6	0.4	0.5
4	0.7	0.3	0.5	0.5	0.5	0.6	0.5	0.5	0.5	0.8
5	0.7	0.4	0	0.6	0.6	0.4	0.6	0.5	0.6	0.7

Table VII *Means of measured values for dentine apposition at point 2 for interval 3 (8 days) in groups of 5 classes 5-month old normal rats*

Midpoint of groups of classes	Number of observations (n)	Mean	SD
3	22	13.5	
8	10	14.6	
13	19	15.1	
18	16	15.7	
23	11	17.5	
28	12	[illegible]	$0.8\sqrt{n}$
33	13	18.5	
38	10	18.5	
43	10	18.6	
48	10	18.5	
53	11	18.3	
58	11	[illegible]	
63	14	16.4	$1.8\sqrt{n}$
68	9	16.0	
3	5	14.6	
	Total 183		

Table V *Calculated values for dentine apposition at each of the 10 points in each of the sets Right side 5 month old normal rats Figures in brackets denote number of animals Cf Table XXV*

Measuring point	1	2	3	4	5	6	7	8	9	10
Set 3—4	19 2	15 3	19 0	14 8	11 7	12 8	12 8	11 8	9 7	12 6
	22 1	18 4	21 0	19 0	16 5	14 7	17 5	14 2	15 7	18 9
	19 2 (18)	18 3 (18)	18 8 (17)	18 4 (17)	16 4 (16)	13 3 (16)	17 7 (12)	13 0 (14)	16 0 (16)	18 0 (17)
	10 8	15 2	12 4	12 8	11 3	8 6	13 4	8 3	10 6	9 7
Set 4—5	9 7	7 3	8 4	6 7	5 2	5 9	5 5	5 3	4 5	5 9
	11 1	8 9	10 9	9 6	7 9	7 5	8 6	7 3	7 7	9 2
	10 [illegible] (11)	9 1 (12)	11 1 (11)	10 1 (12)	8 5 (12)	7 5 (13)	9 6 (11)	7 0 (11)	8 6 (11)	9 9 (11)
	7 8	8 0	9 0	8 3	7 2	6 0	8 0	6 2	7 1	7 8
	3 0	5 6	4 6	4 1	3 8	3 0	5 5	3 0	3 2	3 0
Set 3	19 3	14 8	17 3	13 6	11 2	12 0	12 4	12 6	10 2	13 0
	21 2	16 7	20 2	17 3	14 9	15 0	15 2	14 4	12 5	15 3
	22 4 (14)	17 9 (15)	21 7 (14)	19 4 (14)	16 8 (12)	15 9 (11)	17 5 (8)	15 0 (7)	15 2 (11)	17 9 (12)
	22 7	18 4	21 8	20 0	17 2	14 6	19 3	14 4	18 6	21 1
Set 4	21 3	17 3	21 5	18 4	15 4	15 7	15 6	15 3	13 5	16 2
	22 [illegible]	18 8	21 4	19 9	17 3	15 2	17 0	14 9	16 7	19 [illegible]
	20 4 (16)	18 8 (16)	20 2 (16)	19 4 (15)	16 9 (15)	14 0 (15)	18 4 (14)	13 6 (15)	17 0 (15)	19 2 (15)
	14 9	17 3	17 8	16 9	14 3	12 2	18 1	11 4	14 6	15 4
Set 5	23 9	18 9	22 4	21 5	18 6	16 4	18 8	16 3	17 7	[illegible]1 0
	19 2	18 [illegible]	18 9	18 1	16 3	13 3	17 5	13 [illegible]	16 0	18 4
	13 1 (14)	15 9 (16)	14 4 (14)	14 0 (15)	12 4 (14)	10 0 (1[illegible])	15 1 (15)	10 2 (1[illegible])	12 2 (15)	13 0 (15)
	5 6	11 3	8 9	8 2	7 1	6 [illegible]	11 8	6 2	6 4	4 9

Table X

Source of variation	Set 3				4				5			
	Right		Left		Right		Left		Right		Left	
	m sq	d f	m sq	d f	m sq	d f	m sq	d f	m sq	d f	m sq	d f
T	15 5	6	1 6	6	50 4	8	90 4	5	196 4	7	5.3	5
I	3649	3	3607	3	10560	3	5121	3	42 0.2	3	32522	3
P	2 0.8	9	3395	9	1836	9	1569	9	1090	9	1517	4
TI	212	18	68	18	688	24	61.5	15	20.8	21	253	15
TP	60	54	6.5	54	9.3	72	64	45	11.3	63	101	45
IP	129	27	99	27	229	27	142	27	244	2	181	27
TIP	2.3	162	2 3	162	3 9	216	3 2	135	4 4	189	3.5	135
R	1.2	2 9	0.8	279	1 4	359	1 1	239	1.8	319	1 3	239

Table XI *Calculated values for dentine apposition for 10 measuring points taken together 10 month old rats low weight Figures in brackets denote number of animals*

Set 3—4		4—5		3		4		5	
Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
—	—	6	7 0	14 0	13 9	17 4	17 1	18 6	18 2
14 6	14 0	8 5	8 5	16 3	16 6	18 5	17 9	15 6	14 4
17 8	17 6 (6)	8 6 (3)	8 3 (6)	17 4 ( )	17 6 ( )	17 0 (9)	16 6 (6)	11 7 (8)	10 7 (6)
16 4	16 3	6 9	6 5	17 3	16 9	12 9	13 0	6 9	6 2
10 6	10 1	3 5	3 0	—	—	—	—	—	—

Table XII *Standard deviations of values in Table XI*

Set 3—4		4—5		3		4		5	
Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
1	1.3	1 0	0	1 1	1 1	1 1	1 2	1.3	1.3

Tables XIII–XIV *Analysis of covariance 11 month old normal rats*

Table XIII

Source of variation	Set 3—4				4—5			
	Right		Left		Right		Left	
	m sq	d f	m sq	d f	m sq	d f	m sq	d f
T	10	3	21 9		3 3	4	10.3	3
S	1293 2	3	16.3	3	3 5	4	2 39	4
t	1810	9	100.5	3	23 4	9	23.2	9
TS	21	27	20.8	21	8 8	16	3 3	12
Tt	50	81	6	63	1	36	1.5	2
St	30 6	2	30.5	2	1	36	5 9	36
TSt	3.3	13	2 9	183	1 3	144	0 9	108
R	0 6	399	0.5	319	0.5	219	0 4	190

Table VIII *Means of measured values for dentine apposition at poi... for intervals 2, 4 and 5 pulp (4 days) in groups of 5 classes 5 mo... old normal rats*

Midpoint of groups of classes	Number of observations (n)	Mean value	SD
3	44	6 6	
8	33	7 3	
13	28	7 5	
18	23	7 9	
23	20	8 3	
28	31	8 6	0 6 √n
33	25	9 0	
38	21	9 4	
43	21	9 7	
48	19	9 5	
53	40	9 0	
58	26	9 2	
63	34	9 1	
68	19	9 1	1 2 √n
73	30	8 7	
78	24	7 0	
83	36	5 6	
88	18	5 4	
93	7	4 6	
	Total 499		

Tables IX—X Analysis of covariance 10 month old rats low weigh...

Table IX

Source of variation	Set 3—4 Right m sq	d f	Left m sq	d f	4—5 Right m sq	d f	Left m sq	d f
T	22 9	6	55 1	[illegible]	0 4	2	11 5	[illegible]
S	1167 0	3	1034 1	3	232 0	4	325 3	4
P	102 2	9	216 2	9	19 1	9	53	9
TS	65 1	18	54 4	15	15 2	8	20 0	20
TP	6 7	54	4 1	45	2 4	18	1 2	45
SP	24 8	27	27 2	2	[illegible]	36	8	36
TSP	3 8	162	3 2	135	1 4	72	1 0	180
R	0 8	270	0 6	239	0 6	140	0 3	[illegible]

Table X

Source of variation	Set 3 Right m sq	d f	Left m sq	d f	4 Right m sq	d f	Left m sq	d f	5 Right m sq	d f	Left m sq	d f
T	15.5	6	1 6	6	504	8	904	5	1964	7	5.3	5
I	3649	3	3607	3	10560	3	5121	3	42 02	3	3952 2	3
P	0.8	9	339.5	9	1836	9	1 69	9	1090	9	151[illegible]	9
TI	242	18	26.8	18	58.8	24	61.5	15	20.8	21	253	1[illegible]
TP	6 0	54	6.5	54	3.3	[illegible]	6 4	45	11.3	63	10 1	45
IP	129	27	9 9	27	229	27	14 2	27	24 4	27	18 1	27
TIP	2 3	16[illegible]	2 3	162	3 3	216	3 2	135	4 4	189	3 5	135
R	1.2	2 9	0 8	279	1 4	355	1 1	239	1 8	319	1 3	239

Table XI *Calculated values for dentine apposition for 10 measuring points taken together 10 month old rats low weight Figures in brackets denote number of animals*

Set 3–4 Right	Left	4–5 Right	Left	3 Right	Left	4 Right	Left	5 Right	Left
	—	6	10	14 0	15 9	17 4	17 1	18 6	18 2
14 6	14 0	8 5	8	16.3	16 6	18 5	17 9	1 6	14 [illegible]
1 8 (7)	17 6 (6)	8 5 (3)	8 3 (6)	17 4 ( )	17 6 (7)	17 0 (9)	16 6 (6)	11 7 (8)	10 [illegible] (6)
16 4	16 3	6 5	6 5	17 3	16 5	12 9	13 0	6 9	6 2
10 6	10 1	3 5	3 0	—	—	—	—	—	—

Table XII *Standard deviations of values in Table XI*

Set 3–4 Right	Left	4–5 Right	Left	3 Right	Left	4 Right	Left	5 Right	Left
1 2	1.3	1 0	0 7	1 1	1 1	1 1	1 2	1.3	1.3

Tables XIII—XIV *Analysis of covariance 11 month old normal rats*

Table XIII

Source of variation	Set 3–4 Right m sq	d f	Left m sq	d f	4–5 Right m sq	d f	Left m sq	d f
T	9 0	9	219	[illegible]	33	4	10.3	3
S	1993 2	3	16.3	3	37 .5	4	2 89	4
I	1610	9	160 5	0	234	3	232	0
TS	24	2	70.8	21	8 8	16	3 3	1
TI	5 0	81	6	63	1	36	1 5	2
SI	30 6	[illegible]	30.5	2	1	36	5 9	36
TSI	1.3	213	2 3	193	1 3	144	0 9	108
R	0 6	309	0 5	319	0.5	249	0 4	190

Table VIII *Means of measured values for dentine apposition at point 2 for intervals 2, 4 and 5 pulp (4 days) in groups of 5 classes 5 month old normal rats*

Midpoint of groups of classes	Number of observations (n)	Mean value	SD
3	44	6 6	
8	33	7 3	
13	28	7 5	
18	23	7 9	
23	20	8 3	
28	31	8 6	
33	25	9 0	0 6 √n
38	21	9 4	
43	21	9 7	
48	19	9 5	
53	40	9 0	
58	26	9 2	
63	34	9 1	
68	19	9 1	
73	30	8 7	1 2 √n
78	24	7 0	
83	36	5 6	
88	18	5 4	
93	7	4 6	
	Total 499		

Tables IX—X *Analysis of covariance 10 month old rats low weight*

Table IX

Source of variation	Set 3—4				4—5			
	Right		Left		Right		Left	
	m sq	d f	m sq	d f	m sq	d f	m sq	d f
T	22 9	6	55 1	5	0 4	2	11 5	[illegible]
S	1167 9	3	1034 1	3	232 0	4	325 3	4
P	162 2	9	216 2	[illegible]	19 1	3	53 [illegible]	3
TS	65 1	18	54 4	15	15 2	8	20 0	20
TI	6 [illegible]	54	4 1	45	2 1	18	1 2	45
SP	24 8	27	27 2	27	2 [illegible]	36	8 [illegible]	36
TSI	3 8	162	3 2	135	1 4	72	1 0	180
R	0 8	279	0 6	23[illegible]	0 6	149	0 3	299

Table XVIII

Source of variation	Set 5 Right m sq	d f	Left m sq	d f	6 Right m sq	d f	Left m sq	d f
T	3?	4	58	?	5? 1	7	27 9	7
I	691.2	3	874 5	3	5140 8	3	?515.5	3
J	110 9	9	6? 5	9	[illegible]	?	180 6	9
TI	3? 6	12	1 .3	6	45 5	21	23 6	1
TJ	4 7	3?	2 5	18	5 3	63	6 9	63
IJ	28.3	?7	15 0	2	54 ?	27	?? 0	2
TIJ	5.5	108	5 7	54	?	189	4 ?	189
R	1 ?	199	1 4	119	1	319	1.5	319

Table XIX *Calculated values for dentine apposition for 10 measuring points taken together Young normal rats Age at beginning of experiment 30 days Figures in brackets denote number of animals*

Set 3—4 Right	Left	4—5 Right	Left	5 Right	Left	6 Right	Left
—	—	? 9	8 0	15 7	15 1	18 6	16 8
15 9	1? 2	9	9 7	19	20.8	?0 5	20 5
18 9 (11)	19 1 (9)	9 8 (10)	9 8 (10)	1? 3 ([illegible])	?0 (3)	17 0 (8)	18 6 (8)
19 3	0 0	8 0	8 3	14 4	13 1	8 1	11 ?
1 1	18 9	4.5	5 1	—	—	—	—

Table XX *Standard deviations for values in Table XIX*

Set 3—4 Right	Left	4—5 Right	Left	5 Right	Left	6 Right	Left
?8	0 9	0 5	0	1.3	1.5	1 0	1 0

Table XXI *Calculated values for dentine apposition at each of the 10 measuring points in set 4—5 right side 15 young normal rats*

Measuring point	1	2	3	4	5	6	7	8	9	10
	10 9	9	10.5	8 6	6.8	6 4	6.8	7.0	6 0	7.3
	11.3	9 1	11.8	10 7	8 9	8 6	8 4	8.8	8 7	9 9
Set 4 5	10 ?	9 0	11 4	10 8	5.3	9 0	8 9	8 9	9 4	10.3
	8	6	9 2	8.8	8 0		9.2	7.5	8 0	8.5
	3 0	5 0	5 1	4 9	5.0	4 6	6 ?	4 4	4 7	4.5

Table XIV

Source of variation	Set 3				4				5			
	Right		Left		Right		Left		Right		Left	
	m sq	d f	m sq	d f	m sq	d f	m sq	d f	m sq	d f	m sq	d f
T	85.6	7	24.1	7	24.7	9	31.5	10	99.2	8	103.4	9
I	503.2	3	598.2	3	340.6	3	424.4	3	3244.7	3	3999.[illegible]	3
P	225.7	9	227.6	9	148.1	9	166.2	9	107.6	9	176.7	9
TI	16.1	21	15.9	21	27.8	27	17.7	30	26.1	24	17.[illegible]	27
TP	7.9	63	8.5	63	9.0	81	9.2	90	7.4	72	13.9	81
IP	13.2	27	11.0	27	29.0	27	14.8	27	15.9	27	30.8	27
TIP	2.5	189	2.2	189	3.7	243	2.5	270	5.9	216	6.2	243
R	1.2	319	1.0	319	1.3	399	2.0	439	1.5	359	1.3	399

Table XV *Calculated values for dentine apposition for 10 measuring points taken together 11-month old normal rats Figures in brackets denote number of animals*

Set 3—4		4—5		3		4		5	
Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
—	—	7.1	6.6	14.0	13.5	16.7	16.5	17.3	17.5
14.7	14.8	8.9	8.9	16.3	16.1	18.2	17.8	16.0	16.1
17.9	18.0	8.9 (5)	9.2 (4)	17.5 (8)	17.5 (8)	17.7 (10)	17.1 (11)	12.8 (9)	12.8 (10)
17.0 (10)	17.7 (8)	7.1	7.6	17.7	17.9	15.1	14.4	7.7	7.4
11.9	13.7	3.6	4.0	—	—	—	—	—	—

Table XVI *Standard deviations of values in Table XV*

Set 3—4		4—5		3		4		5	
Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
0.8	0.9	0.6	0.7	1.0	0.[illegible]	0.8	0.7	1.0	1.0

Tables XVII—XVIII *Analysis of covariance Young normal rats Age at beginning of experiment 30 days*

Table XVII

Source of variation	Set 3—4				4—5			
	Right		Left		Right		Left	
	m sq	d f	m sq	d f	m sq	d f	m sq	d f
T	74.4	10	60.6	8	11.2	14	20.8	11
S	387.9	3	240.7	3	1133.9	4	665.9	4
P	277.7	9	28[illegible].0	9	95.1	9	[illegible]0.0	9
TS	19.8	30	23.7	24	8.8	56	12.0	44
TP	3.6	90	3.2	72	1.3	126	1.[illegible]	[illegible]9
SP	44.7	2	21.1	27	23.7	36	8.3	36
TSP	2.8	270	2.5	216	1.0	504	1.2	396
R	0.6	439	0.7	359	0.4	7[illegible]	0.5	[illegible]9

Table XVIII

Source of variation	Set 5 Right m sq	d f	Left m sq	d f	6 Right m sq	d f	Left m sq	d f
T	3[illegible]	4	[illegible]8	[illegible]	[illegible]61	7	2[illegible]9	[illegible]
I	6012	3	8 45	3	1408	3	[illegible]15[illegible]	3
P	1109	9	6[illegible]	9	[illegible]	9	1806	9
TI	366	12	1 3	6	4[illegible]	1	[illegible]36	21
TI	4[illegible]	36	[illegible]	18	[illegible]3	63	69	63
II	28.3	[illegible]	1 0	2	[illegible]16	[illegible]	2[illegible]0	[illegible]
TIP	[illegible]	108	5	[illegible]4	[illegible]6	189	4[illegible]	189
R	12	199	14	119	1	319	1[illegible]	319

Table XIX *Calculated values for dentine apposition for 10 measuring points taken together Young normal rats Age at beginning of experiment 30 days Figures in brackets denote number of animals*

Set 3—4 Right	Left	4—5 Right	Left	5 Right	Left	6 Right	Left
—	—	[illegible]	80	157	151	186	168
15[illegible]	1[illegible]2	9	9	19	[illegible]08 (3)	205	[illegible]05
1[illegible]9	1[illegible]1 (9)	98 (10)	98 (10)	193 ([illegible])	[illegible]0	[illegible]0 (8)	186 (8)
193 (11)	[illegible]00	80	83	144	131	81	112
1 1	189	45	51	—	—	—	—

Table XX *Standard deviations for values in Table XIX*

Set 3—4 Right	Left	4—5 Right	Left	5 Right	Left	6 Right	Left
[illegible]8	09	0.5	0.5	1.3	1.5	10	1.0

Table XXI *Calculated values for dentine apposition at each of the 10 measuring points in set 4—5 right side 15 young normal rats*

Measuring point	1	2	3	4	5	6	7	8	9	10
	109	79	10.[illegible]	86	68	64	6.8	70	60	7.3
Set 4—5	11.3	91	11.8	10	89	8[illegible]	84	88	8	99
	102	90	114	108	9.3	90	8.9	89	94	103
	[illegible]6	[illegible]6	[illegible].2	89	80	[illegible]	8.2	[illegible]5	80	8.5
	39	30	51	49	[illegible]0	46	[illegible]	44	4	4.5

Table XIV

Source of variation	Set 3				4				5			
	Right		Left		Right		Left		Right		Left	
	m sq	d f	m sq	d f	m sq	d f	m sq	d f	m sq	d f	m sq	d f
T	85 6	7	24 1	7	24 7	9	31 5	10	99 2	8	103 4	9
I	503 2	3	598 2	3	340 6	3	424 4	3	3244 7	3	3999 2	3
P	225 7	9	227 6	9	148 1	9	166 2	9	107 6	9	1[illegible]6 7	9
TI	16 1	21	15 9	21	27 8	27	17 7	30	26 1	24	1[illegible] 7	2[illegible]
TP	7 9	63	8 5	63	9 0	81	9 2	90	7 4	72	13 9	81
IP	13 2	27	11 0	27	29 0	27	14 8	27	15 9	2[illegible]	30 8	27
TIP	2 5	189	2 2	189	3 7	243	2 5	270	5 9	216	6 2	243
R	1 2	319	1 0	319	1 3	399	2 0	439	1 5	359	1 3	399

Table XV *Calculated values for dentine apposition for 10 measuring points taken together 11 month old normal rats Figures in brackets denote number of animals*

Set 3—4		4—5		3		4		5	
Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
—	—	7 1	6 6	14 0	13 5	16 7	16 5	1[illegible] 3	17 5
14 7	14 8	8 9	8 9	16 3	16 1	18 2	17 8	16 0	1[illegible] 1
17 9 (10)	18 0 (8)	8 9 (5)	9 2 (4)	17 5 (8)	17 [illegible] (8)	17 [illegible] (10)	17 1 (11)	12 8 (9)	12 8 (10)
17 0	17 [illegible]	7 1	7 6	17 7	17 9	15 1	14 4	7 7	7 4
11 9	13 7	3 6	4 0	—	—	—	—	—	—

Table XVI *Standard deviations of values in Table XV*

Set 3—4		4—5		3		4		5	
Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
0 8	0 9	0 6	0 7	1 0	0 9	0 8	0 7	1 0	1 0

Tables XVII—XVIII *Analysis of covariance Young normal rats Age at beginning of experiment 30 days*

Table XVII

Source of variation	Set 3—4				4—5			
	Right		Left		Right		Left	
	m sq	d f	m sq	d f	m sq	d f	m sq	d f
T	74 4	10	60 6	8	11 2	14	20 8	11
S	387 9	3	240 7	3	1133 [illegible]	4	6[illegible] 9	4
P	277 7	9	282 0	9	[illegible] 1	9	[illegible]0 0	9
TS	19 8	30	23 7	24	8 8	[illegible]	12 0	44
TI	3 6	90	3 2	[illegible]2	1 3	1[illegible]	1 [illegible]	[illegible]
SP	44 7	27	21 1	27	23 7	3[illegible]	8 3	36
TSP	2 8	2[illegible]0	2.5	216	1 0	[illegible]01	1 [illegible]	3[illegible]
R	0 6	439	0 [illegible]	359	0 4	[illegible]49	0[illegible]	[illegible]

Table XXX Means of measured values at each of the measuring points in the 5 sets right side only , month old normal animals (cf Table X which gives the corresponding values calculated with the polynomial

Measuring point	1		3	4	5	6	7	8	9	10
S t 3—4	19 3 21 5 18 19 5 10 7	15 4 17 J 18 18 8 15 0	18 9 1 1 17) 18 12 3	14 8 18 9(17) 18 f 12 9	11 8 1(1(1f) 1f 8 11 7	1 8 14 f(16) 13 4 8 5	17 0 10 9(12) 18 4 13 2	11 9 14 1(14) 13 3 8 4	J 1 1 1(1f) 10 7 10 4	12 9 18 0 18 J(17) 9 5
S 1 4—5	9 8 10 6 11 2 11 3 3 1	8 7 8 9(12) 8 7 5 4	8 5 10 6 11 3(11) J 0 4 5	6 8 9 3 10 2(12) 9 5 4 0	5 4 7 4 8 8(12) 7 3 3 C	5 8 7 9 (3(13) 5 J 3 1	5 8 (7 10 2(11) 8 5 9	J) 7 4 7 9(11) 5 8 3 2	4 8 (9 9 1(11) 7 4 3 1	(4 7 1 10 8(11) (7 2
S t 1	10 2 21 3 22 2(14) 7	14 J 1f 7 19 0(15) 18 4	17 1 0 8(14) 21 4 21 9	13 6 17 3 19 4(14) 0 0	11 2 15 0 16 7(12) 1 2	11 7 15 8(11) 15 1 14 0	12 3 15 8 17 0(8) 19 5	12 1 15 7(7) 13 7 14 9	10 3 12 4(11) 1J 4 18 5	13 0 15 2(12) 18 0 21 0
S t t	21 3 22 5 20 4(16) 14 9	17 3 18 9 18 8(6) 17 4	21 4 21 8 1 J(16) 17 0	18 4 20 0 19 3(15) 16 9	15 5 17 1(15) 17 1 14 3	15 7 15 1 14 1(1) 1 1	15 6 17 3(14) 18 7 18 0	15 4 14 7(1) 13 9 11 3	13 4 16 8 16 9(15) 14 7	10 3 19 1 1J ((1J) 1 3
S t ›	23 (19) 12 4(14) 3 7	18 8 18 9 15 f(16) 11 5	22 1 20 0 13 3(14) 9 1	21 4 19 8 13 7(13) 8 4	18 4 16 9(14) 11 J 7 3	16 1 14 0 J 3(15) 6 7	18 5 18 3 11 4(1) 11 9	16 1 14 1(15))5 (4	17 5 16 7 11 5(15) 6 7	20 0 0 11 4(1) 5 5

Table XXII *Standard deviation for the values in Table XXI*

Measuring point	1	2	3	4	5	6	7	8	9	10
Set 4—5	0.4	0.3	0.3	0.4	0.3	0.2	0.3	0.3	0.3	0.3

Table XXIII *Means of measured values for dentine apposition at point 2 for interval 3 (8 days) in groups of 5 classes Young normal rats*

Midpoint of groups of classes	Number of observations (n)	Mean	SD
3	22	14.9	
8	16	16.6	
13	21	17.9	
18	19	18.8	$1.0\ \sqrt{n}$
23	18	18.4	
28	24	17.2	
33	17	15.4	
38	8	13.8	
	Total 145		

Table XXIV *Means of measured values for dentine apposition at point 2 for interval 4 in groups of 5 classes Young normal rats*

Midpoint of groups of classes	Number of observations (n)	Mean	SD
3	17	6.4	
8	20	7.6	
13	9	8.0	
18	18	8.7	$0.6\ \sqrt{n}$
23	13	9.2	
28	15	9.4	
33	18	9.2	
38	23	8.0	
43	25	6.1	
48	29	4.9	
53	8	4.3	$1.0\ \sqrt{n}$
	Total 195		

Table XXX Means of measured values at each of the measuring points in the 5 sets right side only 5 month old normal animals (of Table) which gives the corresponding values calculated with the polynomial

Measuring point	1	2	3	4	5	6	7	8	9	10
Set 3–4	17 3 21 8 (16) 19 5 10	15 4 17 9 (18) 18 8 15 0	18 9 1 1 (17) 18 12 3	14 8 18 9 (17) 18 6 12 9	11 9 10 1 (16) 10 8 11 3	12 8 14 6 (11) 13 4 8 5	13 0 16 8 (12) 13 4 13 2	11 9 14 1 (14) 17 3 9 4	3 3 1 1 (10) 16 7 10 4	19 9 18 0 (17) 18 3 9 5
Set 4 5	9 8 10 6 11 (11) 3 3 1	8 9) (1_) 8 7 4	8 5 10 6 11 3 (11) 3 0 4 5	6 9 3 3 10 2 (12) 8 4 0	5 4 7 4 8 8 (12) 7 3 3 6	5 8 7) 3 (13) 5 3 3 1	9 7 10 (11) 8 5 3 3	5 7 4 7 9 (11) 8 3 2	4 8 1 9 3 1 (11) 7 4 1 1	6 4 7 1 10 9 (11) 7 2 7
Set 3	19 2 21 3 (14) 22 2 2 7	14 9 16 7 (1 18 0 18 4	1 1 20 8 (14) 21 4 21 9	13 6 17 3 (14) 19 4 0 0	11 15 0 (12) 16 7 1 2	11 15 8 (11) 1) 14 9	12 3 15 9 (8) 17 0 19 3	1 1 15 7 (7) 13 7 14 9	10 1 1 4 (11) 15 4 18 5	13 0 15 2 (12) 18 0 21 0
Set 4	21 3 22 3 (16) 20 4 14 3	17 3 18 9 18 8 (6) 17 4	21 4 21 8 (16) 19 9 17 3	18 4 20 0 (15) 19 3 16 9	1 5 17 1 (15) 17 1 14 3	15 7 15 1 (15) 14 1 1 1	1 0 1 1 (14) 18 7 18 0	15 4 14 7 (15) 13 3 11 3	13 4 16 8 (1) 16 3 14 7	16 3 19 1 (15) 13 15 3
Set	23 7 13) (14) 1 4 5 7	18 9 18 3 (10) 15 6 11 5	22 1 20 0 (14) 13 3 9 3	21 4 18 8 (1) 13 7 8 4	18 4 16 9 (14) 11 0 7 3	16 1 14 0 (15) 3 6 7	19 5 18 3 (1) 14 4 11 9	10 1 14 1 (15) 5 6 4	17 5 16 7 (15) 11 5 6 7	20 20 0 (1) 11 4 5 5

Table XXII *Standard deviation for the values in Table XXI*

Measuring point	1	2	3	4	5	6	7	8	9	10
Set 4—5	0 4	0 3	0 3	0 4	0 3	0 2	0 3	0 3	0 3	0 3

Table XXIII *Means of measured values for dentine apposition at point 2 for interval 3 (8 days) in groups of 5 classes Young normal rats*

Midpoint of groups of classes	Number of observations (n)	Mean	SD
3	22	14 9	
8	16	16 6	
13	21	17 9	
18	19	18 8	1 0 √n
23	18	18 4	
28	24	17 2	
33	17	15 4	
38	8	13 8	
	Total 145		

Table XXIV *Means of measured values for dentine apposition at point 2 for interval 4 in groups of 5 classes Young normal rats*

Midpoint of groups of classes	Number of observations (n)	Mean	SD
3	17	6 4	
8	20	7 6	
13	9	8 0	
18	18	8 7	0 6 √n
23	13	9 2	
28	15	9 4	
33	18	9 2	
38	23	8 0	
43	25	6 1	
48	29	4 9	
53	8	4.3	1 0 √n
	Total 195		

Table XXX Means of measured values at each of the measuring points in the 5 sets right side only 5 month old normal animals (f Table X which gives the corresponding values calculated with the polynomial

Measuring point	1		3	4	5	6	7	8	9	10
Set 3—4	1?3	15 4	18 9	14 8	11 8	12 8	13 0	11 9	[illegible]	12 9
	21 8	17 9	1 1	18 9	16 1	14 C	16 8	14 1	1 1	18 0
	19 5 (18)	18 8 (18)	18 ? (17)	18 C (17)	1C 8 (1C)	13 4 (1C)	18 4 (1?)	13 3 (14)	16 7 (16)	18 ? (17)
	10 7	15 0	1 3	12 9	11 3	8 ?	13 2	8 4	10 4	15
Set 4—5	9 8	7	8 ?	6 8	5 4	5 8	5 8	5 2	4 8	C 4
	10 6	8 7	10 6	9 3	7 4	? 9	? ?	7 4	? 9	7 ?
	11 (11)	8 9 (1)	11 3 (11)	10 2 (12)	8 8 (12)	7 3 (13)	10 ? (11)	7 9 (11)	9 1 (11)	10 8 (11)
	? 3	8 7	9 0	8	7 ?	5 9	8 5	8	7 4	? 7
	3 1	? 4	4 5	4 0	3 6	3 1	3	3 2	3 1	2 7
Set 3	19 2	14 9	17 1	13 6	11 2	11 7	12 3	1? 1	10 3	13 0
	1 3	16 7	20 C	17 3	15 0	1 8	1 8	15 7	12 4	15
	22 2 (14)	18 0 (15)	21 4 (14)	19 4 (14)	1C 7 (12)	15 1 (11)	17 0 (8)	13 7 (7)	1 4 (11)	18 0 (12)
	7	18 4	21 ?	?0 0	1? 2	14 9	1?	14 9	19 5	21 0
Set 4	21 3	17 3	21 4	18 4	1 5	15 7	15 6	1 4	13 4	16 3
	2	18 ?	21 8	?0 0	17 1	?5 1	1? ?	14 7	1C 8	19 1
	0 4 (16)	18 8 (6)	19 9 (16)	19 3 (15)	17 1 (1)	14 1 (15)	18 7 (14)	13 ? (?)	16 ? (15)	1? ? (1?)
	14 9	17 4	17 9	16 9	14 3	1? 1	18 0	11 3	14 7	1 3
Set 5	23 7	18 9	22 1	21 4	18 4	16 1	18 5	16 1	17	20
	1? ?	18 9	?0 0	18 8	16 9	14 0	18 3	14 1	16 7	20 0
	12 4 (14)	15 6 (16)	13 3 (14)	13 7 (1?)	11 9 (14)	? 3 (15)	14 4 (1?)	? 5 (15)	11 5 (15)	11 4 (1)
	5 7	11 5	9 3	8 4	7 3	6 7	11 9	C 4	6 7	5 ?

Tables XXVI—XXVII *Analysis of covariance 4 month old rats Treatment with growth hormone during latter half of experimental period*

Table XXVI

Source of variation	Set 3—4 Right m sq	d f	Left m sq	d f	4—5 Right m sq	d f	Left m sq	d f
T	20.5	6	30.8	4	5.8	4	13.0	2
S	849.1	3	841.4	3	3?1.0	4	200.7	4
P	228.5	9	117.9	9	26.1	9	15.2	9
TS	36.2	18	42.1	12	6.7	16	19.0	8
TP	2.2	54	2.7	36	1.5	36	2.9	18
SP	30.2	27	26.7	27	9.9	36	5.2	36
TSP	2.7	162	1.8	108	1.2	144	1.2	72
R	0.5	2?9	0.5	199	0.4	249	0.5	149

Table XXVII

Source of variation	Set 3 Right m sq	d f	Left m sq	d f	4 Right m sq	d f	Left m sq	d f	5 Right m sq	d f	Left m sq	d f
T	0.9	3	26.8	2	1?2	9	2?8	9	53.5	9	14?.0	8
I	524.5	3	448.7	3	307.3	3	372.1	3	2719.8	3	2517.8	3
P	176.7	9	118.3	9	230.4	9	261.9	9	171.5	9	160.9	9
TI	4.4	9	8.6	6	67.2	27	86.4	27	10?.4	27	70.4	24
TP	2.6	27	4.5	18	5.9	81	7.6	81	6.3	81	7.4	72
IP	13.4	27	8.2	27	33.0	27	29.0	27	41.6	27	29.7	27
TIP	2.7	81	1.3	54	3.7	243	4.2	243	5.3	243	4.5	21?
R	0.9	159	0.7	119	1.1	399	1.0	399	1.4	399	1.2	3?9

Table XXVIII *Calculated values for dentine apposition for 10 measuring points taken together 4 month old animals Treatment with growth hormone during latter half of experimental period Figures in brackets denote number of animals*

Set 3—4 Right	Left	4—5 Right	Left	3 Right	Left	4 Right	Left	5 Right	Left
—	—	?.0	6.4	12.8	12.3	15.?	15.?	18.1	1?.8
14.1	13.9	8.9	8.9	1?.?	15.? (3)	17.8	1?.7 (10)	1?.5 (10)	1?.? (9)
18.1	18.4	9.0 (5)	9.5 (3)	17.? (4)	17.2	18.1 (10)	18.2	14.8	15.0
17.9 (7)	17.9 (5)	?.2	8.1	18.7	18.5	16.7	1?.0	?.9	9.8
13.5	12.?	?.5	4.8	—	—	—			—

Table XXIX *Standard deviations of values in Table XXVIII*

Set 3—4 Right	Left	4—5 Right	Left	3 Right	Left	4 Right	Left	5 Right	Left
1.1	1.3	0.7	1.0	1.5	1.?	0.9	1.0	1.2	1.1

Table XXX Calculated values for dentine apposition at each of the 10 points in the sets Right side 4 month old animals Treatment with growth hormone during latter half of experimental period Figures in brackets denote number of animals

Measuring point	1	2	3	4	5	6	7	8	9	10
Set 3—4	18 5 2 2 21 2 (10) 15 5	14 3 17 4 (10) 18 5 17 4	18 2 21 2 20 2 (10) 15 0	14 7 19 2 19 3 (9) 15 1	11 9 1(5 17 1 (8) 13 7	12 4 15 9 15 2 (7) 10 2	12 2 10 6 17 8 (7) 15 9	12 4 1 6 1 0 (7) 10 6	10 6 10 3 17 1 (7) 13 0	13 1 18 2 (9) 18 14 5
Set 4—5	9 10 7 10 (7) 7 (2 9	7 2 8 9 9 3 (7) 8 5 6 4	8 7 10 6 10 6 (7) 8 4 4 3	7 0 3 3 6 (7) 7 9 4 4	5 8 9 1 8 6 ( ) 7 1 3 8	6 2 7 9 7 ( ) 6 2 2 9	6 1 8 4 9 0 ( ) 8 1 5 6	(8 0 8 1 ( ) 6 4 2 9	4 9 7 7 8 6 (6) 7 4 4 1	6 3 2 7 (7) 8 0 3 9
Set 3	17 5 19 6 21 1 ( ) 22 0	13 5 15 1 16 3 (9) 18 9	15 9 1 8 21 9 (7) 0 1	12 7 16 1 18 3 (6) 13 5	9 7 13 7 16 1 (5 16 7	10 3 14 2 16 2 (5) 16 1	10 7 13 16 8 (4) 19 3	11 4 14 0 15 (4) 15 9	9 1 3 15 2 (4) 17 7	11 9 14 4 17 6 (6) 21 4
Set 4	19 2 1 6 20 (10) 16 4	15 5 17 7 18 9 (10) 19 1	19 9 20 7 0 0 (10) 17 8	16 5 18 9 18 9 (10) 16 7	14 4 16 1 16 5 (10) 15 6	14 8 15 8 15 3 (10) 13	14 3 16 18 0 (10) 19 0	15 2 16 16 1 (10) 14	1 0 15 17 4 (10) 16 7	14 2 18 0 13 (10) 17 7
Set	21 5 20 4 15 7 (10) 7 4	18 1 18 8 17 1 (10) 13	0 5 18 5 14 8 (10) 9 6	13 2 18 2 15 4 (10) 10 9	17 7 17 14 7 (10) 9 2	15 14 4 1 0 (10) 8 1	17 8 17 5 16 4 (10) 14 7	15 7 14 (10) 12 8 5	11 3 16 5 14 2 (10) 9 5	18 3 18 5 13 (10) 9 7

Table XXXI *Standard deviations for the values in Table XXX*

Measuring point	1	2	3	4	5	6	7	8	9	10
Set 3—4	0 8	0 4	0 6	0 8	0 7	0 6	0 8	0 5	0 8	0 9
4—5	0 7	0 6	0 5	0 5	0 5	0 4	0 5	0 4	0 4	0 6
3	0 8	0 4	0 6	0 7	1 0	0 8	0 6	0 7	0 7	0 6
4	1 0	0 5	0 5	0 7	0 8	0 7	0 7	0 7	0 8	0 8
5	1 3	0 9	0 9	1 1	1 0	0 8	1 1	1 0	0 9	1 1

Table XXXII *Means of measured values in different intervals and groups of classes 4 month old animals No treatment Control experiments*

Midpoint of groups of classes	Interval 1		2		3		4	
	No of observations (n)	Mean	No of observations (n)	Mean	No of observations (n)	Mean	No of observations (n)	Mean
3	17	10 1	13	9 9	16	9 9	19	9 7
8	13	10 5	7	11 0	11	10 6	12	11 6
13	13	11 5	11	11 5	15	11 4	17	11 1
18	15	11 7	11	12 1	5	12 6	8	12 4
23	11	12 3	5	13 8	10	13 6	15	13 1
28	11	13 5	13	13 6	15	14 1	10	13 3
33	16	13 8	7	14 3	3	15 0	[illegible]	14 0
38	3	12 7	3	15 0	11	14 5	13	14 4
43	13	13 3	13	14 4	9	14 1	10	14 4
48	8	13 4	10	13 9	7	13 6	7	13 4
53	5	13 6	3	13 7	6	13 0	10	13.3
58	—	—	12	12 9	13	13 3	14	13 5
63	2	13 0	6	13 3	10	13 1	8	10 9
68	1	11 0	—	—	10	10 9	8	10 9
73	—	—	1	9 0	9	9 3	11	9 4
78	—	—	2	8 5	2	6 5	3	6 7
83	—	—	—	—	1	12 0	4	8 2
88	—	—	—	—	1	[illegible]	—	—
Total	128	—	11	—	154	—	174	—

Table XXXIII *Means of measured values in different intervals and groups of classes 4 month old animals Treatment with growth hormone during latter half of experimental period Control experiments*

Midpoint of groups of classes	Interval 1		2		3		4	
	No of observations (n)	Mean	No of observations (n)	Mean	No of observations (n)	Mean	No of observations (n)	Mean
3	1	9 6	15	9 9	1	10 0	8	10 2
8	12	10 7	13	10 9	13	11 5	19	10 9
13	13	11 1	9	11 3	10	11 6	9	11 6
18	12	12 0	13	11 9	7	12 7	11	11 6
23	8	12 9	5	12 8	13	13 3	14	12 6
28	15	12 9	5	13 4	8	14 4	7	13 7
33	9	14 0	8	14 1	7	15 0	11	14 4
38	13	13 5	12	14 0	6	14 5	10	14 3
43	11	14 0	9	13 6	9	14 4	7	14 1
48		13 3	8	13 6	8	14 8	8	14 2
53	8	13.5	13	13	11	14 1	7	14 0
58	2	11 5	10	12 6	6	13 5	10	13 9
63	—	—	8	13 0	10	12 8	6	12 7
68	—	—	7	11 0	10	12.3	17	11.2
3	—	—	1	11 0	9	10 3	6	9.2
8	—	—	—	—	1	9 0	10	7 6
83	—	—	—	—	1	0	3	7 0
88	—	—	—	—	—	—	1	0
Total	125	—	144	—	141	—	164	—

Table XXXI *Standard deviations for the values in Table XXX*

Measuring point	1	2	3	4	5	6	7	8	9	10
Set 3—4	0 8	0 4	0 6	0 8	0 7	0 6	0 8	0 5	0 8	0 9
4—5	0 7	0 6	0 5	0 5	0 5	0 4	0 5	0 4	0 4	0 6
3	0 8	0 4	0 6	0 7	1 0	0 8	0 6	0 7	0 7	0 6
4	1 0	0 5	0 5	0 7	0 8	0 7	0 7	0 7	0 8	0 8
5	1 3	0 9	0 9	1 1	1 0	0 8	1 1	1 0	0 9	1 1

Table XXXII *Means of measured values in different intervals and groups of classes 4 month old animals No treatment Control experiments*

Midpoint of groups of classes	Interval 1		2		3		4	
	No of observations (n)	Mean	No of observations (n)	Mean	No of observations (n)	Mean	No of observations (n)	Mean
3	17	10 1	13	9 9	16	9 9	19	9 7
8	13	10 5	7	11 0	11	10 6	12	11 6
13	13	11 5	11	11 5	15	11 4	17	11 1
18	15	11 7	11	12 1	5	12 6	8	12 4
23	11	12 3	5	13 8	10	13 6	15	13 1
28	11	13 5	13	13 6	15	14 1	10	13 3
33	16	13 8	7	14 3	3	15 0	5	14 0
38	3	12 7	3	15 0	11	14 9	13	14 4
43	13	13 3	13	14 4	9	14 1	10	14 4
48	8	13 4	10	13 9	7	13 6	7	13 4
53	5	13 8	3	13 7	6	13 0	10	13.3
58	—	—	12	12 9	13	13 3	14	13 5
63	2	13 0	6	13 3	10	13 1	8	10 9
68	1	11 0	—	—	10	10 9	8	10 9
73	—	—	1	9 0	9	9 3	11	9 4
78	—	—	2	8 5	2	6 5	3	6 7
83	—	—	—	—	1	12 0	4	8 2
88	—	—	—	—	1	5 0	—	—
Total	128	—	117	—	151	—	174	—

Table XXXV *Analysis of covariance Young animals Treatment with growth hormone during latter half of experimental period*

Source of variation	Set 4—5 Right m sq	d f	Source of variation	Set 6 Right m sq	d f
T	16.4	22	T	32.9	14
S	13 0.5	4	I	4203.1	3
I	146.3	9	P	256.1	9
TS	13.7	88	TI	55.5	42
TP	1.5	198	TP	5.6	126
SP	16.8	36	IP	66.3	27
TSP	1.2	792	TIP	4.0	378
P	0.5	1140	R	1.4	599

Table XXXVI *Calculated values for dentine apposition for 10 measuring points taken together Young animals Treatment with growth hormone during latter half of experimental period*

Set	4—5 Right	6 Right
Section or interval	—	16.8
	8.3	20.5 (12)
	10.1	18.8
	10.2 (10)	11.7
	8.5	—
	5.2	—

Table XXXVII *Calculated values for dentine apposition at each of the 10 measuring points set 4—5 right side 23 young animals Treatment with growth hormone during latter half of experimental period*

Measuring point	1	2	3	4	5	6	7	8	9	10
Set 4—5 right side	10.4	8.6	10.2	8.9	7.4	7.4	7.2	7.4	6.8	8.0
	11.9	9.5	11.5	10.9	9.4	9.1	9.1	9.3	9.3	10.2
	11.6	9.4	11.8	11.2	9.9	9.3	9.6	9.5	10.1	10.6
	9.4	8.1	9.5	9.7	8.7	8.1	8.6	8.1	9.0	9.1
	5.5	5.8	6.3	6.4	6.1	5.5	6.1	4.9	6.2	5.9

Table XXXVIII *Standard deviations of values in Table XXXVI*

Set	4—5 Right	6 Right
	0.5	0.9

Table XXXIV. *Means of measured values in different intervals and groups of classes. 4 month old animals. Treatment with solvent for growth hormone during latter half of experimental period. Control experiments*

Midpoint of groups of classes	Interval 1		2		3		4	
	No of observations (n)	Mean	No of observations (n)	Mean	No of observations (n)	Mean	No of observations (n)	Mean
3	12	9.7	15	9.7	19	9.9	11	9.[illegible]
8	7	10.4	8	10.9	15	11.2	20	11.0
13	15	11.3	13	11.8	19	11.3	16	11.1
18	10	12.0	11	12.1	8	12.6	11	12.3
23	5	13.2	10	12.6	15	13.2	21	12.8
28	14	13.7	14	13.9	16	13.9	9	12.9
33	8	14.1	6	14.0	5	14.0	11	14.4
38	6	13.8	11	14.1	15	13.9	10	14.7
43	8	13.7	13	14.4	14	14.0	14	14.4
48	5	13.4	10	13.2	5	13.6	9	14.1
53	3	14.7	9	13.8	16	14.3	12	13.8
58	2	13.0	7	14.0	15	13.4	13	13.2
63	1	12.0	5	13.2	13	12.6	9	11.3
68	1	12.0	5	12.8	11	10.4	16	12.1
73	1	7.0	2	10.5	6	11.3	8	10.7
78	—	—	—	—	7	10.3	5	8.2
83	—	—	2	11.0	3	7.7	4	5.7
88	—	—	—	—	—	—	1	8.0
Total	98	—	141	—	202	—	200	—

Table XLII *Means and numbers of measured values in different intervals and groups of classes Young animals Treatment with solvent for growth hormone during latter half of experimental period*

Midpoint of groups of classes	Interval 1		2		3		4	
	No of observations	Mean	No of observations	Mean	No of observations	Mean	No of observations	Mean
3	24	15 8	18	6 6	16	14 6	16	7.2
8	15	18 5	20	8 0	22	16 6	6	7.5
13	—	—	14	8 9	17	18 2	13	8 0
18	—	—	15	9 8	18	18 9	11	8 7
23	—	—	12	10 4	12	19 7	15	9 6
28	—	—	10	10 6	18	18 8	13	9 4
33	—	—	—	—	12	17.2	12	9 4
38	—	—	—	—	8	15.2	17	9 0
43	—	—	—	—	1	17 0	16	6 7
48	—	—	—	—	—	—	18	6 1
3	—	—	—	—	—	—	5	5 2
8	—	—	—	—	—	—	2	4.5
Total	39	—	89	—	124	—	144	—

Table XLIII *Analysis of covariance 4 month old animals Treatment with cortisol during latter half of experimental period*

Source of variation	Set 4		5			
	Right		Right		Left	
	m sq	d f	m sq	d f	m sq	d f
T	32 1	3	151 4	3	22.2	3
I	2 09	3	1255 4	3	1036.2	3
I	34 3	9	39 8	9	34.5	9
TI	9 8	9	102 6	15	57.8	9
TI	11 7	27	10 1	45	9 2	27
II	29 1	2	31.3	2	21 9	2
TIP	8 1	81	8 0	135	5 9	81
R	1 2	159	1 9	239	1	159

Table XXXIX *Standard deviations for values in Table XXXVIII*

Measuring point	1	2	3	4	5	6	7	8	9	10
	0.4	0.2	0.3	0.3	0.3	0.2	0.2	0.2	0.3	0.3

Table XL *Means and numbers of measured values in different intervals and groups of classes Young animals No treatment*

Midpoint of groups of classes	Interval 1		2		3		4	
	No of observations	Mean	No of observations	Mean	No of observations	Mean	No of observations	Mean
3	27	15.6	18	7.2	22	14.9	17	6.4
8	17	17.8	17	8.3	16	16.6	20	7.5
13	1	17.0	13	8.8	21	17.9	9	8.0
18	—	—	21	9.5	19	18.8	18	8.7
23	—	—	12	9.9	18	18.4	13	9.2
28	—	—	9	9.9	24	17.2	15	9.4
33	—	—	—	—	17	15.4	18	9.[illegible]
38	—	—	—	—	8	13.8	23	8.0
43	—	—	—	—	—	—	25	6.1
48	—	—	—	—	—	—	29	4.9
53	—	—	—	—	—	—	9	4.3
58	—	—	—	—	—	—	1	3.0
Total	45	—	90	—	145	—	197	—

Table XLI *Means and numbers of measured values in different intervals and groups of classes Young animals Treatment with growth hormone during latter half of experimental period*

Midpoint of groups of classes	Interval 1		2		3		4	
	No of observations	Mean	No of observations	Mean	No of observations	Mean	No of observations	Mean
3	53	15.5	36	7.2	39	15.4	32	7.2
8	12	17.4	40	8.3	33	17.4	21	8.1
13	1	19.0	41	9.2	32	19.2	29	8.7
18	—	—	34	9.7	37	19.4	[illegible]	9.5
23	—	—	25	10.0	33	19.8	28	9.0
28	—	—	4	9.7	30	18.2	21	9.[illegible]
33	—	—	1	10.0	28	17.0	35	9.[illegible]
38	—	—	—	—	[illegible]	[illegible]	27	8.9
43	—	—	—	—	1	14.0	42	6.9
48	—	—	—	—	—	—	45	5.[illegible]
53	—	—	—	—	—	—	11	4.4
58	—	—	—	—	—	—	—	—
Total	66	—	181	—	238	—	316	—

Table XLVIII *Means and numbers of measured values in different intervals and groups of classes 4 month old animals Treatment with cortisol during latter half of experimental period Control experiments*

Midpoint of groups of classes	Interval 1		2		3		4	
	No of observations (n)	Mean	No of observations (n)	Mean	No of observations (n)	Mean	No of observations (n)	Mean
3	13	9.8	17	10.0	18	10.3	18	10.1
8	18	10.4	14	10.8	7	10.4	9	10.6
13	12	10.6	6	11.5	12	10.7	14	10.4
18	17	11.7	16	12.0	11	11.2	10	10.4
23	1	12.4	11	12.2	8	12 [illegible]	6	8.7
28	15	12.8	10	13.1	9	12.3	8	8.7
33	15	13.8	13	13.9	9	13.1	7	10.0
38	6	13.7	11	13.6	9	13.1	6	9.3
43	7	13.4	10	13.5	7	12.6	3	7.3
48	2	14.0	12	13.2	14	11.9	9	9.9
53	—	—	5	12.2	9	10.6	5	8.6
58	—	—	6	13.0	5	11.0	8	8.1
63	—	—	1	13.0	11	10.6	7	7.6
68	—	—	—	—	2	9.5	3	6.3
3	—	—	—	—	2	9.0	2	6.5
8	—	—	—	—	—	—	2	5.5
83	—	—	—	—	—	—	—	—
88	—	—	—	—	—	—	—	—
Total	117	—	132	—	133	—	117	—

Table XLIV *Calculated values for dentine apposition for 10 measuring points taken together 4 month old animals Treatment with cortisol during latter half of experimental period*

	Right	Left
Set 4	14 4	
	16 5	
	15 9 (4)	
	12 6	
Set 5	16 4	17 3
	16 7	17 5
	14 5 (6)	15 1 (4)
	9 7	10 2

Table XLV *Standard deviations of values in Table XLIV*

Set 4	5	
Right	Right	Left
1 6	1 5	1 4

Table XLVI *Calculated values for dentine apposition Measuring point 2 right side 4 month old animals Treatment with cortisol during latter half of experimental period Figures in brackets denote number of animals*

Set 3—4	3	4	5
12 8	12 0	15 1	17 5
15 8	14 6	17 4	17 5
16 3 (7)	15 1 (6)	16 4 (8)	15 [illegible] (11)
14 4	13 6	12 2	12 5

Table XLVII *Standard deviations of values in Table XLVI*

Set	3—4	3	4	5
	0 7	0 7	0 8	0 7

Table IL *Means and numbers of measured values in different intervals and groups of classes Treatment with suspension medium for cortisol during latter half of experimental period Control experiments*

Midpoint of groups of classes	Interval 1		2		3		4	
	No of observations (n)	Mean	No of observations (n)	Mean	No of observations (n)	Mean	No of observations (n)	Mean
3	16	10 1	11	10 0	5	9 6	4	9 [illegible]
8	10	11 0	9	11 1	10	10 8	14	10 9
13	12	11 1	14	11 5	11	11 4	6	11 [illegible]
18	12	11 9	10	12 6	8	12 0	9	1[illegible] 1
23	11	12 9	8	12 6	10	13 2	13	1[illegible] 5
28	11	13 7	9	13 3	9	13 1	6	13 [illegible]
33	9	13 7	7	14 1	10	13 9	7	13 7
38	11	13 9	10	13 9	6	14 2	9	14 2
43	7	13 9	6	13 8	9	13 4	7	14 0
48	8	13 6	6	13 2	8	13 4	9	13 6
53	2	14 0	10	13 0	8	12 9	7	1[illegible] 7
58	2	12 5	5	11 8	9	12 8	7	12 9
63	1	12 0	4	12 7	6	10 7	10	1[illegible] 2
68	—	—	3	11 3	9	10 7	5	11 6
73	—	—	—	—	2	11 0	14	8 6
78	—	—	1	9 0	3	10 7	5	6 6
83	—	—	—	—	1	9 0	4	8 0
88	—	—	—	—	—	—	2	7 0
Total	112	—	113	—	124	—	138	—

HENRYK TKACZUK

TENSILE PROPERTIES OF HUMAN LUMBAR LONGITUDINAL LIGAMENTS

Acta Orthopaedica Scandinavica
Supplementum No 115
Munksgaard Co [illegible] 68

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Tensile Properties of Human Lumbar Longitudinal Ligaments

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From the Department of Orthopaedic Surgery University of Gothenburg Sweden
(head. Professor Carl Hirsch)

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BY

HENRYK TKACZUK

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II REVIEW OF LITERATURE

Historical review of literature

In 1845 Purkinje and in 1858 von Luschka gave a detailed description of the disc, its embryology as well as the innervation of the posterior longitudinal ligaments through the sinuvertebral nerve (the nerve of Luschka) Virchow writing in 1872 ascribed afflictions of the vertebral column to asthenia and in 1881 Beneke included asthenia in constitutional disorders Kretschmer in 1907 studied the asthenic weakness of ligaments but finally asthenia was defined as the imperfect development of the connective tissue within the whole organism Schmorl and Junghanns in 1932 in their classic work on the vertebral column have a detailed description of the structure of ligaments The posterior longitudinal ligament they described as narrower and thinner than the anterior longitudinal ligament Schmorl referring to Fick (1904) said that the posterior longitudinal *ligament is also more elastic and that on flexion the posterior longitudinal* ligament was compressed against the vertebral bodies thus occluding all underlying vascular structures Schmorl in his description of the vessels which enter the posterior aspect of vertebral body mentioned the nerve of Luschka and pointed out that irritation of this nerve could be a cause of pain in the region of the vertebral column

In 1940 Roofe using the silver stain method demonstrated unmyelinated nerve endings in the posterior longitudinal ligament The innervation of the posterior longitudinal ligament has also been investigated by Wiberg (1949) Hirsch (1951) Pedersen Blunck and Gardner (1956) Stilwell in 1956 gave a very detailed description of the innervation of the anterior longitudinal ligament in a monkey Magnuson (1944) demonstrated that if one injected physiological saline into the ligament surrounding the intervertebral foramen one may produce pressure on the root ganglia and thus cause pain Hirsch in 1948 and in 1963 injected physiological saline into lumbar discs and reproduced pain *characteristic* of clinical low back pain Inman and Saunders (1942 1944 and 1947) stressed the role which ligaments play in the mechanics *of the spine* and considered that low back pain was caused by irritation of the nerves of the longitudinal ligaments

Willis in 1941 considered the various possible causes of low back pain and felt that one of the most important factors was overloading of the longitudinal ligaments This statement was based *on* congenital deformations of the vertebral column

Haboush in 194? studied the order in which ligaments tore on forceful flexion of the vertebral column He determined that the posterior longitudinal ligament as well as the lateral portions of the anterior longitudinal ligament burst or tore

I INTRODUCTION

The ligaments of the locomotor system have as their function the joining of the bony elements where they are normally subjected to tension Their functional prerequisite is that they act as elastic structures Ageing as well as degenerative changes may alter the mechanical characteristics of ligaments

For years investigators have speculated on which structures in the lumbar spine may produce low back pain Many have focused their attention on the discs others have investigated joints (Lewin 1964) and ligaments of the spine Tensile properties of interspinous ligaments and of the ligamentum flavum have been tested (Akerblom 1948 Newman 1952 Silver 1954 Nunley 1958 Rissanen 1960 Rolander 1966 Nachemson and Evans 1967) but there is a lack of information on the physical properties of the anterior and posterior longitudinal ligaments

In this work the author has endeavoured to answer the following questions

a) What are the tensile characteristics of the longitudinal ligaments of the lumbar spine?
b) Has age any influence on the tensile properties of the longitudinal ligaments?
c) Have degenerative changes of the lumbar spine any influence on the tensile properties of the longitudinal ligaments?

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tissue As a protein it belongs to the group of sclero-proteins and comprises 1/3 of the protein of a human being Grassman in 1965 gave perhaps the best characterization of collagen as a substance in his opening address at St Andrew s when he stated Collagen indeed is a peaceful protein which is not as active as its prominent brother myosin which is needed to raise the sword Collagen causes no wounds but it heals wounds

Collagen is produced by the fibrocytes which in turn are surrounded closely by the collagen fibres The collagen fibres are built up from amino-acids in the following order glycine proline hydroxyproline glycine (Hall 1965) The hydroxyproline which comprises about 20 per cent of the amino-acids found in collagen is considered to be responsible for the resistance of the collagen fibre to various chemical substances (Gross 1961 Hall 1965) The solubility properties of collagen allow collagen to be divided into three fractions (Harkness 1961 and 1966 S F Jackson 1964) These fractions are

1) The saline soluble fraction
2) The acid soluble fraction
3) The insoluble fraction

The fraction which is saline soluble is the one found in young collagen or in collagen structures with a rapid metabolic turn over e g the uterus during pregnancy (Hall 1965) The acid soluble fraction also belongs to young collagen The greatest portion of connective tissue however is made up of the insoluble fraction of collagen which characterizes mature connective tissue (Gallop 1964 Hall 1965 Piez 1966) The soluble fractions of collagen, with ageing undergo a change and become insoluble (Gross 1952 Banga 1966)

The amino acids aggregate to form molecules of collagen which are also *known* as tropo collagen The molecular weight of collagen is in the region of 350 000 The molecule is 2800 Å in length and about 15 Å in width (Hall 1965 Harkness 1966)

There is a number of theoretical models illustrating the molecular structure of collagen (Gross 1952 Gustavsson 1956 Schmitt and Hodge 1960 Harkness 1961 Ramachandran 1962) The most popular theoretical model is a helix coiled to the left which is comprised of *three fractions* alfa beta and gamma and the whole structure in turn is in the form of a *superhelix* or *trihelix*, coiled to the right The forces which bind the superhelix together are not fully known The assumption is that there are hydrogen *bonds between the* alfa, beta and gamma fractions (Hall 1965 Banga 1966) The molecules *are joined* end to end and in this way give rise to protofibrils which have the same linear orientation and are bound to each other by electrostatic forces (Schmitt and Hodge 1960) Of note however is the fact that the molecules *are staggered* overlapping each other by one quarter of their length Thus in a 2800 Å section this staggering repeats itself four times approximately 700 Å *apart, and is* visible in the electronmicroscope as the dark cross bands The fibrils which are made up of protofibrils are *within the*

Allbrook in 1957 analyzing the cause of anterior lipping felt that it formed as a result of traction at the attachment of the anterior longitudinal ligament to the vertebral bodies

O Connell in 1951 felt that low back pain may be caused by partial tearing or by stretching of ligaments The relaxation of ligaments is in O Connell s opinion caused by a hormone produced by the corpus luteum (relaxin) during pregnancy which may be the cause of unremitting low back pain during pregnancy particularly if the woman has to do hard work

Harris and MacNab (1954) link the degenerative changes in the intervertebral disc with changes taking place in the ligaments particularly the longitudinal ligaments and ligamentum flavum

Leikkonen, in 1959 in his discussion of disc pathology stated that the posterior longitudinal ligament could be stretched by the bulging nucleus pulposus

In 1962, Arutynow basing his contentions on observations made at surgery concluded that degenerative changes are not confined to the disc but also involve the posterior longitudinal ligament and the ligamentum flavum

Cremonese and Tomatis in 1963 stated that nerve impulses which originate from irritation of the posterior longitudinal ligament via the sinuvertebral nerve of Luschka cause in severe cases a protective muscle spasm This enlarges the intervertebral space on the side of the disc herniation and thus diminishes the force on the disc producing at the same time the so called sciatic scoliosis as well as straightening of the lumbar lordosis

Roaf in 1960 claimed that he was not able to disrupt the no mal anterior longitudinal ligaments on flexion or extension of the lumbar spine as the bone fractured On the other hand rotation easily damages the ligaments He felt that degenerative changes have no influence on either the posterior or anterior longitudinal ligaments

Hackett in 1961 felt that excessive stretching of the ligaments stimulates their sensory nerves which via a sympathetic reflex cause neuro vascular disturbances in the region of the bone This in turn results in decalcification and thus weakens the insertion of other ligaments In this way a vicious circle is established

Hirsch (1954 and later) discussed the degeneration and deformation of the disc which causes it to interfere with the longitudinal ligaments and thus irritates their nerves as being a possible cause of pain

General properties of collagen and ground substance

COLLAGEN

The chief components of ligaments are collagen and ground substance The physical properties of most ligaments are determined by the collagen component The collagen is not only the framework of all ligaments but also of all connective

The first account of the elastic properties of different human tissue was published by Wertheim in 1847 This investigator noted that the deformation of the tissues was not proportional to the loading The curve constructed on the basis of load and deformation had the shape of a hyperbola In addition Wertheim stated that the curve was described by a second degree equation $Y^2 = ax^2 + bx$ This relationship has since been substantiated by many investigators (Annovazzi 1928 Gratz 1931 Akerblom 1948 Stucke 1950 Dick 1951 Rigby 1964 Viidik 1965—66 Kenedi Gibson and Daly 1965) but their interpretation of the physical properties differ considerably

It is generally agreed that ligaments exhibit visco-elastic behaviour A material is called visco-elastic if its properties are some combination both of a solid and of a fluid (Ferry 1961 Fredrikson 1964 Frost 1967)

If one wishes to utilize a classical model of a visco-elastic structure then biological material seems to fit most closely to the Voigt Kelvin element This is a material in which the stress is the sum of two parts one proportional to the strain and the other proportional to the strain rate (Ferry 1961 Fredrikson 1964)

In carrying out the loading of a ligament one obtains a curve in which the toe part is concave in the direction of the load axis Subsequently the line described becomes less and less concave and approaches a straight line

When the yield point is reached the curve changes direction into the direction of the strain axis (plastic part) Plastic deformation continues until the breaking point is finally reached

Many authors are of the opinion that the first part of the curve the toe part is dependent on the wavy formation of collagen bundles (Stucke 1950 Rigby 1964 Kenedi et al 1965 Viidik 1966) The curve becomes less concave under the influence of increasing load and when finally the wavy formation disappears and the collagen fibres have assumed an orientation in the lin of stress a straight line is achieved that is the elastic portion of the curve Dick (1951) and Ridge and Wright (1965) studying the elastic properties of skin were of the opinion that the toe part is due to the presence of elastin fibres and the remainder of the curve is representative of collagen The elastic property of collagen is evident in the section of the curve between the toe part and the beginning of the plastic range (Annovazzi 1928 Gratz 1931 Smith 1954 Wright and Rennels 1964) Wright and Rennels (1964) determined that loading a collagen sample to 60—60 per cent (1 8 kg mm2) of the failure load causes a permanent elongation of the specimen Gratz (1931) felt that the maximal loading of human fascia lata, before plastic deformation took place was 1 4 kg mm Smith (1954) studying the cruciate ligaments of the rabbit, found that one could attain the elastic behaviour of the tissue by loading it with the weight of the rabbit over a 5 minute period or with

resolution of the electronmicroscope as they have a width of 500—1000 Å (Schmitt et al 1942 Schmitt 1944 Wassermann 1951 Hall 1965) *The fibrils* in turn are joined to give rise to fibres which are then within the resolution of the ordinary microscope The fibrils appear to be glued to each other by muco polysaccharides *(Banga 1966) The mucopolysaccharides* can be removed by heating (about 60—70°C) and then the collagen changes into a mass of randomly *coiled fibres (Banga 1966 Harkness 1966 Piez 1966) With age* some properties of collagen undergo a change Verzar in 1957 showed that the energy of contraction which the collagen fibres generate under the influence of temperature *is directly proportional to their age The older the collagen the greater the energy* Banga in 1966 found that young collagen is more extensible and has greater *tensile strength than old* tissue Gross in 1952 found that collagen fibres in the young are both thinner and shorter than in the mature Kohn and Rollerson (1958) found that young fibres absorb fluid in greater quantities and more rapidly than old collagen Verzar (1957) and S F Jackson *(1964) found that* during an isotonic contraction older collagen fibres contract more and use up more energy than young ones Jackson considers that the changes which take place in the physical properties of collagen are the result not only of ageing but also of *maturation and are the adjustment to greater stresses It has also been established* that with ageing the amount of ground substance diminishes in favour of an increase in the thickness of the collagen fibres (Catchpole et al 1951 Sobel and Marmorston 1956 Gersh 1959 *Hall 1966*) and the ratio of the mucopolysac *charides to collagen (H/C ratio) is inversely proportional* to age (Sobel and Marmorston (1956)

GROUND SUBSTANCE

The collagen fibres have a close relationship with the ground substance which is comprised *chiefly* of mucopolysaccharides *It is considered that the mucopolysac* charides are produced either in the fibrocytes or in the mast cells (Catchpole et al 1951 Ragan 1952 Jorpes and Yamashima 1956) Meyer in 1956 classified the mucopolysaccharides into sulphated mucopolysaccharides and nonsulphated muco polysaccharides To the sulphated mucopolysaccharides belong the following Chondroitin sulphate *A B C heparine sulphate keratosulphate To the non* sulphated group belong Hyaluronic acid and chondroitin

It is felt that the structure of mucopolysaccharides is in the form of a polymer made up of repeated couplets of two sugars Hyaluronic acid does not branch whereas chondroitin sulphate does branch through the sulphate radical It is *known that chondroitin sulphate links with protein* The combination of muco polysaccharides with protein is in the form of large radicals which contain or trap *large amounts of water within their domains* This in turn influences the physical properties of the connective tissue (Gustavsson 1956 Hall 1965)

Tensile characteristics of collagenous tissues

The first account of the elastic properties of different human tissue was published by Wertheim in 1847 This investigator noted that the deformation of the tissues was not proportional to the loading The curve constructed on the basis of load and deformation had the shape of a hyperbola In addition Wertheim stated that the curve was described by a second degree equation $Y = ax^2 + bx$ This relationship has since been substantiated by many investigators (Annovazzi 1928 Gratz 1931 Akerblom 1948 Stucke 1950 Dick 1951 Rigby 1964 Viidik 1965—66 Kenedi Gibson and Daly 1965) but their interpretation of the physical properties differ considerably

It is generally agreed that ligaments exhibit visco-elastic behaviour A material is called visco-elastic if its properties are some combination both of a solid and of a fluid (Ferry 1961 Fredrikson 1964 Frost 1967)

If one wishes to utilize a classical model of a visco-elastic structure then biological material seems to fit most closely to the Voigt Kelvin element This is a material in which the stress is the sum of two parts one proportional to the strain and the other proportional to the strain rate (Ferry 1961 Fredrikson 1964)

In carrying out the loading of a ligament one obtains a curve in which the toe part is concave in the direction of the load axis Subsequently the line described becomes less and less concave and approaches a straight line

When the yield point is reached the curve changes direction into the direction of the strain axis (plastic part) Plastic deformation continues until the breaking point is finally reached

Many authors are of the opinion that the first part of the curve the toe part is dependent on the wavy formation of collagen bundles (Stucke 1950 Rigby 1964 Kenedi et al 1965 Viidik 1966) The curve becomes less concave under the influence of increasing load and when finally the wavy formation disappears and the collagen fibres have assumed an orientation in the line of stress a straight line is achieved that is the elastic portion of the curve Dick (1951) and Ridge and Wright (1965) studying the elastic properties of skin were of the opinion that the toe part is due to the presence of elastin fibres and the remainder of the curve is representative of collagen The elastic property of collagen is evident in the section of the curve between the toe part and the beginning of the plastic range (Annovazzi 1929 Gratz 1931 Smith 1954 Wright and Rennels 1964) Wright and Rennels (1964) determined that loading a collagen sample to 60—80 per cent (1 8 Kg mm²) of the failure load causes a permanent elongation of the specimen Gratz (1931) felt that the maximal loading of human fascia lata before plastic deformation took place was 1 4 Kg mm² Smith (1954) studying the cruciate ligaments of the rabbit found that one could attain the elastic behaviour of the tissue by loading it with the weight of the rabbit over a 5 minute period or with

resolution of the electronmicroscope as they have a width of 500—1000 A (Schmitt et al 1942 Schmitt 1944 Wassermann 1951 Hall 1965) The fibrils in turn are joined to give rise to fibres which are then within the resolution of the ordinary microscope The fibrils appear to be glued to each other by muco polysaccharides (Banga 1966) The mucopolysaccharides can be removed by heating (about 60—70°C) and then the collagen changes into a mass of randomly coiled fibres (Banga 1966 Harkness 1966, Piez 1966) With age some properties of collagen undergo a change Verzar in 1957 showed that the energy of contraction which the collagen fibres generate under the influence of temperature is directly proportional to their age The older the collagen the greater the energy Banga in 1966 found that young collagen is more extensible and has greater tensile strength than old tissue Gross in 1952 found that collagen fibres in the young are both thinner and shorter than in the mature Kohn and Rollerson (1958) found that young fibres absorb fluid in greater quantities and more rapidly than old collagen Verzar (1957) and S F Jackson (1964) found that during an isotonic contraction older collagen fibres contract more and use up more energy than young ones Jackson considers that the changes which take place in the physical properties of collagen are the result not only of ageing but also of maturation and are the adjustment to greater stresses It has also been established that with ageing the amount of ground substance diminishes in favour of an increase in the thickness of the collagen fibres (Catchpole et al 1951 Sobel and Marmorston 1956 Gersh 1959 Hall 1966) and the ratio of the mucopolysac charides to collagen (H/C ratio) is inversely proportional to age (Sobel and Marmorston (1956)

GROUND SUBSTANCE

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momentary submaximal loads In biological materials such as the ligaments two time dependent phenomena appear namely the creep and the relaxation phenomenon The gradual approach to limiting extension (strain) under a constant force (stress) is called creep (Ferry 1961, Fredrikson 1964) The gradual reduction in force (stress) exerted by a body under a fixed amount of compression or extension is called relaxation (Ferry 1961 Fredrikson 1964) Both these phenomena exist in the living tissues and make the testing of the physical properties of ligaments very difficult The curves which one obtains by consecutive loading of the ligament are not identical (Viidik 1967, Galante 1967)

COLLAGEN IN AGEING

Collagen is a protein which may be described as "old in that sense that with ageing it undergoes slow changes in its metabolic turn over (Banga 1966) Wertheim (1847) found that the 'stiffness of tissue increases with age Annovazzi (1928) found that ligaments from young animals were more deformable than ligaments of older animals A similar observation was made by Banga (1966) who described young collagen tissue as more stretchable and more resistant to tearing Gustavsson (1956) stated that connective tissue of mature animals contained more collagen Ingelmark (1948) proved that with ageing collagenous tissues lose water regardless of their function Katzenstein and Fecher (1924) described the ligaments of the human knee as less deformable after the age of 40 years Curtis (1963) while studying the modulus of elasticity found that ligaments of older people were more rigid particularly under slow rates of straining Galante (1967) studying the physical properties of the annulus fibrosus showed that there is an age difference in the elastic properties of the annulus He stated *that elongation residual deformation and energy dissipation decreased progressive*ly until the age of 26 after which they remained practically constant

The investigators who looked into the problem of ageing of connective tissue used different techniques Many studies were carried out on the solubility properties of collagen in different substances (Harkness 1961 Hall 1965 Banga 1966) The first one who determined the correlation between contractability of collagen under the influence of temperature and the relationship of this with *ageing was Verzar (1957) The contractile property of young and old collagen* under the influence of concentrated solutions of urea was studied by Elden (1965) Banga (1966) tried to age collagen on the basis of potassium iodide staining Kratky Lauer, Ratzenhofer and Sekora (1962) studied the age dependence of human tendon collagen using X ray diffraction They found a difference between the X ray diffraction patterns of young and old collagen Rigby (1964) comparing young and old collagenous tissues investigated their physical properties by determining the strain stress curves X ray diffraction patterns and shrinkage temperatures He determined that ligaments of older people have greater resistance to strain their X ray diffraction pattern showed less distinct wavy formation and

their shrinkage temperature was higher Sylven Paulson Hirsch and Snellman (1951) studying the properties of the nucleus pulposus by electronmicroscopy found that with ageing the three dimensional lattice gel system containing a dense network of collagen fibrils and amorphous interfibrillar substance irregularly loses the amorphous mucoid material and the fibrils become visible The above authors were of the opinion that this mucoid interfibrillar material contained a large quantity of water The decrease with ageing in the amount of this mucoid material results in a decrease in the water content and thus influences the physical properties of this tissue

POST MORTEM CHANGES

The question of how rapidly the mechanical behaviour of collagen tissues changes post mortem has been of great interest to many investigators and to date the question has remained unresolved Wertheim (1847) investigated tendons nerves and arteries of dogs immediately and five days after death He determined that no differences in the tensile properties of the tissues took place Annovazzi (1928) found that the physical properties of the cruciate ligaments of the canine knees change immediately after death and even more so in the next ten hours Gratz (1931) while studying the human fascia lata preserved in physiological saline for 18 hours concluded that it seemed to be essentially alive Kenedi et al (1965) using a bioengineering approach to the study of human skin could not find a noticeable difference in the tensile properties of the skin in vivo or in vitro Viidik Sandqvist and Magi (1965) on the basis of detailed studies of the cruciate ligaments of the rabbit came to the conclusion that no distinct changes in the tensile characteristics of the tissue occur within the first 96 hours after death The authors concluded that the greatest cause of the change in the tensile properties of the tissue was dehydration

The condition for maintaining the physical properties of the ligaments was preservation of the intact and closed knee joint until the test was performed Hirsch and Galante (1967) tried to determine the loss of water from the moment of death to the time of testing by determining the weight of the intervertebral disc of rabbits immediately after death and after 48 hours They found that the difference between the two groups was not significant It may be however that the change in the physical properties of ligaments takes place almost with the last heart beat and this may in some way change the hydromechanical property of the collagen tissue Thereafter other changes take place really very slowly and depend chiefly on the loss of water

III ANATOMY OF THE LONGITUDINAL LIGAMENTS OF THE HUMAN LUMBAR SPINE

The longitudinal ligaments are *situated directly on the posterior* and *anterior* aspects of the vertebral bodies and thus join the adjacent vertebrae (Fig 1) Accurate descriptions of the ligaments if one disregards the old classical anatomical texts were given by Fick (1904) Strasser (1908) Schmorl and Junghanns (1932) Rauber Kopsch (1932), Hirsch and Schajowicz (1952)

ANTERIOR LIGAMENT

The anterior longitudinal ligament constitutes a strong band which covers the anterior aspect of the lumbar spine as well as some of the antero lateral aspect The ligament has a firm attachment to the vertebral bodies particularly at their edges *The average width of the ligaments*, measured during this study in 35 autopsy specimens in the age range 20 to 67 years, was as follows

L5 2 cm
L3 2 5 cm
L2 2 3 cm

These measurements were carried out at the level of the vertebral bodies At the same levels the average thickness of the ligament was

L5 1 9 mm
L3 2 1 mm
L2 0 9 mm

There is an evident thinning of the anterior longitudinal ligament at the level of the annulus fibrosus The average thickness of the anterior longitudinal ligament at the level of the L4—5 intervertebral disc was 0 8 mm The ligament is easily separated from the underlying annulus fibrosus but is connected to it by fibres which are disposed at right angles to the axis of the anterior longitudinal ligament (Schmorl and Junghanns 1932) *At the level of L3 and L2 the anterior* (i e *the abdominal) surface of the ligament is usually irregular and there are* accessory fibres adjacent to the main portion of the ligament From L2 upwards the ligament becomes thinner and narrower

POSTERIOR LIGAMENT

The posterior longitudinal ligament is narrower and weaker than the anterior longitudinal ligament At the level of L5—S 1 it appears as an irregularly developed oval structure which varies from 2—2 25 mm in width From L5

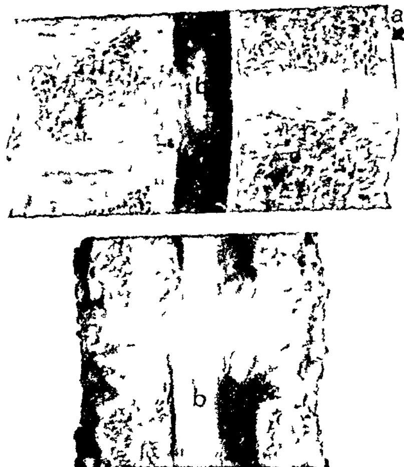


Fig 1 The longitud nal ligaments of the lumbar spine
a) Anterior long tudinal ligament
b) Posterior longitudinal ligament.

upwards the ligament forms a narrow band which widens symmetrically at the level of each disc The ligament is strongly attached to fibres of the annulus fibrosus and to the edge of the vertebral body but very poorly and in some cases not at all to the posterior aspect of the vertebra The average widths of the ligament at the different levels are as follows

L5	1 4 cm disc level
L3	1 5
L2	1 1
L5	0 7 cm vertebral body level
L3	0 8
L2	0 6

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IV MATERIAL AND METHODS

Material

The anterior and posterior longitudinal ligaments were taken from lumbar vertebral columns obtained at post mortem The studies carried out were based on 74 vertebral columns from which 484 samples were taken In addition to the ligaments samples of the annulus fibrosus were obtained for histological studies The specimens were tested within 48 hours of death The ligaments were taken from the segments S 1 to T 12 inclusively and occasionally the 12th thoracic segment was included The annulus fibrosus was sampled from L2 L3 L4 and L5 The condition of the intervertebral disc was assessed on the basis of its macro scopic appearance basing it on the generally accepted criteria (Friberg 1948 Friberg and Hirsch 1949 Virgin 1951 Hirsch and Schajowicz 1952 Ingelmark and Ekholm 1952) which are

Grade 1 The normal disc The annulus fibrosus and the nucleus pulposus are white without a distinct transition as the fibrous structure of the annulus is not visible

Grade 2 The visibility of the fibres of the annulus determines the transition zone between the nucleus and the annulus

Grade 3 Visible fissures in the annulus fibrosus The border between the nucleus and the annulus is no longer distinct The nucleus pulposus is rather dry and at times one can see distinct brown staining the so called brown degenera tion

Grade 4 Marked changes Tears and sequestrations in the region of the annulus and nucleus and brown degeneration deformation of the adjacent bone to the annulus in the form of osteophytes

The anterior longitudinal ligament was removed in the form of a band taken from its mid portion and measuring 2 cm in width The posterior longitudinal ligament was taken in its entirety with the except on that the segments between L5 and S 1 as well as those between T 12 and L 1 because of their size (the liga ment is narrow and thin) were not always suitable for testing. The anterior longitudinal ligament in the segment between L4 and L5 was frequently damaged during autopsy and was not always suitable for testing In addition particularly in children the ligaments in the upper segments were too thin and did not meet our test requirements These segments of the ligaments were not tested but were used for histological examinations The ligaments were taken from the level of the disc as well as from the segment overlying the vertebra. Where possible the fragments of the ligaments which were adjacent to the disc were tested separately Table I lists the specimens tested and Table II shows the number of the different test as well as the numbers of preparations of the ligaments which were used for these tests

The average thickness of the ligaments are as follows

L5 1 3 mm
L3 1 4 ,
L2 0 9 ,

The posterior longitudinal ligament appears to be best developed at the level L3 and L4 where its average thickness is 1 4 mm From L2 upwards the ligame thins markedly Throughout the whole length of the ligament one can note distinctly thicker middle portion approximately 2 5—4 mm in width In cro section the ligament has the form of an elipse In the mid portion of each vertebr body the posterior longitudinal ligament covers the vascular foramina (Schmo and Junghanns 1932)

*The posterior longitudinal ligament is innervated by branches of the sinuvert*bral (or Luschka) nerve This nerve has fibres which connect the nervus spina with the sympathetic ganglia and it enters the intervertebral foramen and divid into ascending and descending branches It gives branches to the vessels and th enters with them into bone through the vascular foramina It also supplies t posterior longitudinal ligament and, to some degree the ligamentum flavu *The anterior longitudinal ligament is supplied by branches which come fro* the sympathetic plexus which is connected with the nervus spinalis (Stilwe 1956) (Fig 2) In contradistinction to other ligaments of the vertebral column which the nerve endings are superficial the anterior longitudinal ligament h nerve endings deeply situated in its substance (Hollinshead 1965)

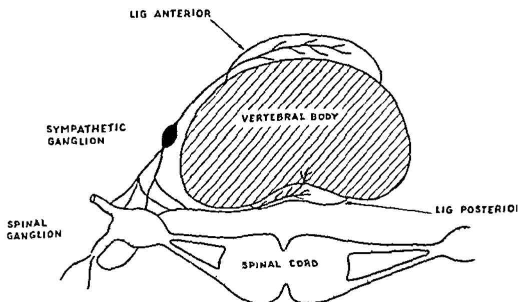


Fig 2 Innervation of the longitudinal ligaments (after Stilwell)

Subject number	Autopsy number	Age years	Sex	Death to testing	Cause of death
45	I 131[illegible]	64	M	2 days	Myocardial infarction
46	I 1051	6[illegible]	F	1 day	Myocardial infarction
47	I 1205	67	F	1	Pulmonary embolism
48	II 279	58	F	8 hours	Carcinoma of the stomach
49	II 243	55	M	1 day	Carcinoma of the bladder
50	I 941	22	M	12 hours	Cardiac failure
51	I 1134	17	M	8	Circulatory failure
52	I 1170	59	F	1 day	Cerebral tumor
53	I 1091	51	F	2 days	Intracranial haemorrhage
54	I 1331	4	F	1 day	Meningitis purulenta
55	I 1276	1 day	F	8 hours	*Hydronephrosis*
56	I 1329	10 days	F	12 hours	Atelect pulm
57	I 1330	17	M	1 day	Immatur
58	I 1228	5 years	F	12 hours	Tumor cerebri
59	I 1317	10 days	F	1 day	Pneumonia
60	I 1293	20	M	8 hours	Pneumonia
61	I 1318	30	M	10	Intracranial haemorrhage
62	I 1281	1 day	M	10	Haemorrhagia pericardii
63	I 1055	57 years	M	2 days	Haemorrhagia cerebri
64	II 235	59	F	1 day	Embolia pulm
65	I 1212	2,5	M	1	Bronchopneumonia
66	I 1444	55	M	2 days	Haemorrhagia cerebelli
67	*I 639*	36	M	10 hours	Uremia
68	I 925	36	F	1 day	Circulatory failure
69	I 616	58	M	8 hours	Bronchopneumonia
[illegible]0	I 1273	54	M	1 day	Carcinoma of the stomach
71	*I 1343*	63	M	2 days	Myocardial infarction
[illegible]	*II* 79	58	M	2	Bronchopneumonia
73	I 57	[illegible]6	F	10 hours	Uremia
[illegible]4	I 1417	64	M	1 day	Myocardial infarction

TABLE 1

Subject number	Autopsy number	Age years	Sex	Death to testing	Cause of death
1	I 600	77	F	1 day	Cardiac failure
2	L.S 59	76	M	1	Bronchopneumonia
3	I 949	60	M	2 days	Subdural haematoma
4	I 586	45	M	1 day	Cardiac failure
5	L 973	51	M	12 hours	Tumor cerebri
6	I 948	42	F	2 days	Carcinoma pancreati
7	I 984	53	F	1 day	Rupt aneur a cerebr med
8	L S 80	55	M	2 days	Acute alcoholic intoxication
9	I 60	36	F	1 day	Tumor cerebri
10	I 1209	48	M	2 days	Tumor cerebri
11	I 777	68	M	2	Cardiac failure
12	L S 56	92	M	1 day	Circulatory failure
13	I 739	59	M	1	Myocardial infarction
14	I 761	62	M	10 hours	Myocardial infarction
15	L 706	82	F	1 day	Cardiac failure
16	I 783	64	F	1	Cardiac failure
17	I 644	45	F	2 days	Rupt aneur a carotis int
18	I 653	51	F	2	Myocardial infarction
19	I 732	20	M	1 day	Contusio cerebri
20	I 698	56	M	1	Cardiac failure
21	L- 771	63	F	2 days	Embolia pulm
22	I 621	38	M	1 day	Embolia cerebri
23	I 679	73	M	2 days	Myocardial infarction
24	I 786	56	F	1 day	Myocardial infarction
25	I 767	58	F	1	Myocardial infarction
26	I 759	35	F	12 hours	Embolia pulm
27	I 428	56	M	1 day	Aneur art cerebri med
28	I 748	70	F	10 hours	Myocardial infarction
29	I 689	55	M	1 day	Myocardial infarction
30	II 148	74	M	2 days	Peritonitis
31	I 178	66	M	1 day	Circulatory failure
32	I S 43	65	F	2 days	Bronchopneumonia
33	I 61	70	M	1 day	Myocardial infarction
34	I 1214	57	M	1	Myocardial infarction
35	I 1037	48	M	12 hours	Peritonitis
36	I 1341	51	F	2 days	Intra abdominal haemorrage
37	I 1229	24	F	12 hours	Pulmonary embolism
38	I 1176	21	F	1 day	Myocarditis
39	I 1056	46	M	1	Cardiac failure
40	I 1108	50	M	1	Respiratory failure
41	I 1054	29	M	1	Peritonitis
42	I 909	33	F	2 days	Uremia
43	I 1178	66	M	1 day	Cardiac failure
44	I 1438	65	F	1	Cardiac failure

Subject number	Autopsy number	Age years	Sex	Death to testing	Cause of death
45	I 1316	64	M	2 days	Myocardial infarction
46	I 1051	66	F	1 day	Myocardial infarction
47	I 1205	67	F	1	Pulmonary embolism
48	II 279	58	F	8 hours	Carcinoma of the stomach
49	II 243	55	M	1 day	Carcinoma of the bladder
50	I 941	22	M	12 hours	Cardiac failure
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71	I 1343	63	M	2 days	Myocardial infarction
72	II [illegible]9	58	M	[illegible]	Bronchopneumonia
73	I 57	26	F	10 hours	Uremia
74	I 1417	64	M	1 day	Myocardial infarction

TABLE II

Number of experiment	Experiment	Number of samples	Specimen Number
1	The water loss of samples exposed to air	15	1 2
2	The swelling of the ant and post ligaments in different solutions	48	5 6 7 8
3	The water loss from samples in the high humidity chamber	20	3 4
4	The influence of rapid freezing and thawing on physical properties of long ligaments	28	9 10 11
5	Studies on the loading capacity of segments of long ligaments of full thickness	22	67 68 72
6	Studies on the loading capacity of samples of equal dimensions from the ant and post long ligaments	30	66 73 74
7	Repetitive loading	116	13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 30 31 32 33
8	Studies to obtain preloading point for the long ligaments	—	65 29 51 47 48 50 43 54 42 73 70 9 71 69
9	Microscopic investigation of ligaments subjected to loading	—	12 51 61
10	Effect of age and degeneration on tensile properties	206	34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64

Methods

At first the ligaments were removed with the aid of a dissection microscope (Zeiss) using 15 fold magnification Experience later showed this to be unnecessary In addition refinements in the preparation technique of the samples minimized damage to the surface of the preparation In order to determine the orientation of the collagen bundles in both the anterior and posterior longitudinal ligaments histological studies were carried out We detected a marked wavy formation but nevertheless the mean orientation of bundles was parallel to the longitudinal axis of the lumbar spine Histological studies of ligaments placed under a certain amount of tensile stress revealed that the collagen bundles straightened and assumed a relationship parallel with one another The anterior

longitudinal ligament as well as the posterior were cut into segments which corresponded to the levels of L1 L2 L3 L4 and L5 Thereafter these were put in clamps and were loaded to the point of tearing These studies showed that the ligaments were visco elastic The load/strain curves were typical of a collagenous structure (Viidik 1966 Galante 1967) It was also possible to conclude that, for comparable tests identical sized samples should be used

PREPARATION OF THE TEST SAMPLE

The ligaments after removal from the vertebral column were cut into segments which corresponded to the levels of the lumbar spine These were then frozen in a carbon dioxide snow stream and were cut on the Jung freezing microtome Special calibration of the microtome allowed us to cut sheets of 0 5 mm thickness During the sectioning the knife of the microtome was so positioned that it was parallel to the direction of the collagen bundles

MEASUREMENTS OF THE THICKNESS OF THE TEST SAMPLE

Great difficulties were encountered in determining the thickness of the test samples because of the visco elastic nature of the tissue At first we tried to measure the frozen samples with a micrometer screw gauge but found that this was very inaccurate as the samples thawed very rapidly and changed in consistency We finally based our measurements on the system introduced by Galante (1967) during his studies of the physical properties of the annulus fibrosus This method consists of a dial displacement gauge with an accuracy of + or — 0 01 mm made by the firm Metron This gives measurements of the thickness of the ligament placed between two metal plates The weight of the plates as well as the pressure of the micrometer piston does not exceed 0 13 gm/mm² which results in a minimal creep of no more than 0 03 mm If the thickness of the test sample showed a difference greater than 5 per cent from the standard thickness or if the thickness of the test sample was not uniform the sample was discarded

METHOD OF OBTAINING IDENTICAL SAMPLES

In order to obtain identical bands of uniform width from the sheets we at first employed a dissection microscope The samples were cut from the sheet under a 15 fold magnification with the aid of a grid graduated in mm which was placed under the sheet We found that the accuracy which one could obtain in this way was not adequate and in addition the time taken to obtain samples was far too long The sample dried a very significant factor as we found in our later experiments We again made use of an instrument introduced by Galante the so called "stamping press which employs two types of dies For experiments in which we tried to determine the breaking point, dies with a narrowed central segment were employed For all other determinations dies of size 30×2 mm were

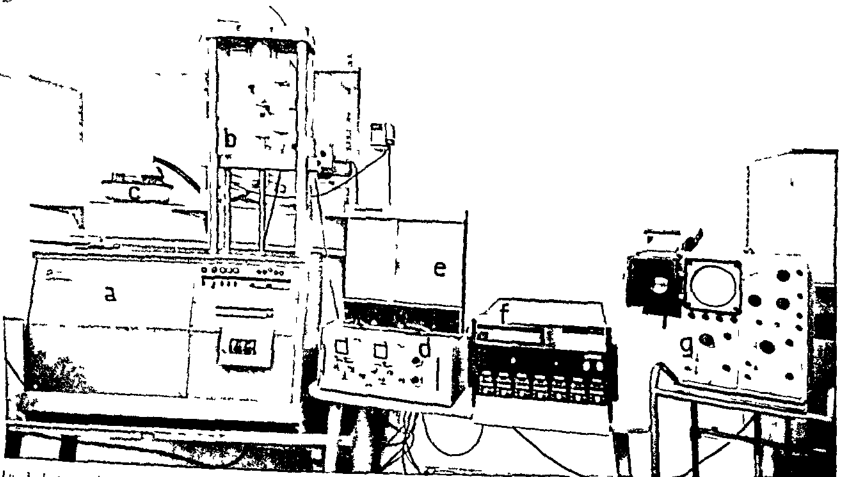


Fig. 3 Te ting and rece rding e juipment (acc rding t Hirsch et al)
a) Alwetr n test machine
b) Test chamber with humidity and temperature sensors
c) Defensor humidif er
d) Ampl fiers
e) XY ecor ler
f) T pe rec d
g) O ll g ph

employed A soft plastic material was placed under the sample which was then stamped with the die A goniometer attached to the base of a rotating wooden disc allowed us to cut the ligaments parallel to the course of the collagen fibres The cutting dies were machined out of steel which were subsequently hardened The cutting edges were sharpened at an angle of 15° In this way we obtained samples of 30 mm length occasionally a little shorter of 0 5 mm in thickness and 2 mm in width The length of the sample was not critical as the distance between the testing clamps during the test was always 9 mm the length width ratio being 4 5 1

TESTING EQUIPMENT

Two types of testing systems were employed in our tests In the initial determinations of the whole ligament we employed the Alwetron Electronic Universal Testing Machine T 2000 coupled to an XY recorder unit Philips Y type We found however that the recording device was inadequate In all other tests we used the following system Alwetron T 2000 coupled to a Hewlett Packard Moseley recorder model AM 7001 or AM 7030 In order to determine the accuracy of the recording device we coupled the system with an oscilloscope (Textronix type I AG) equipped with a Polaroid camera (Fig 3 and 4) The curves obtained with the recorder were compared to those obtained with the oscilloscope and they were found to be identical In trying to determine the breaking point we employed a 50 Kg load cell with a 0 1 per cent accuracy In the other experiments we used a 1 Kg load cell with a 005 per cent accuracy The rate of loading was varied from 0 5 mm min to 50 mm,min Most tests were conducted at a strain rate of 5 mm min

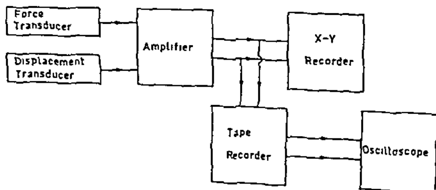


Fig 4 Block diagram of the recording system

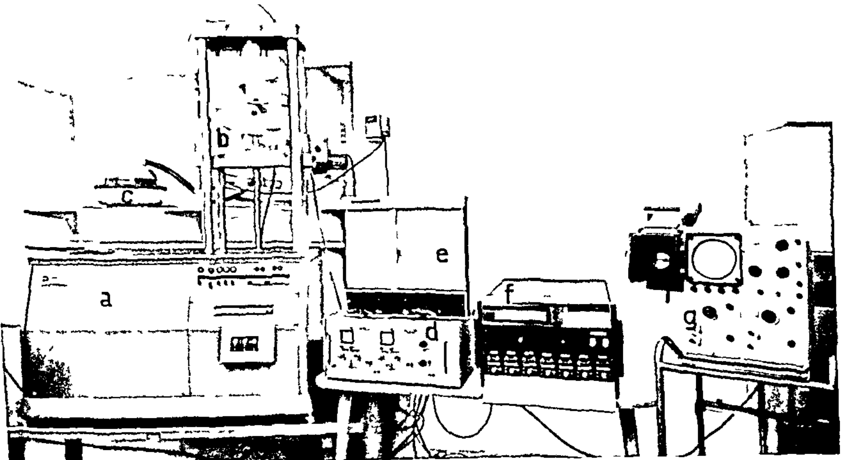


Fig. 3 Testing and recording equipment (according to Hirsch et al.)
a) Alwetron test machine
b) Test chamber with humidity and temperature sensors
c) Defensor humidifier
d) Amplifiers
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f) Tape recorder
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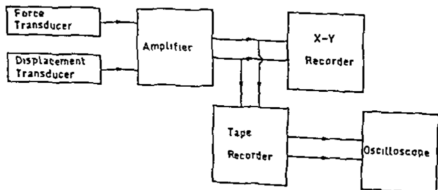


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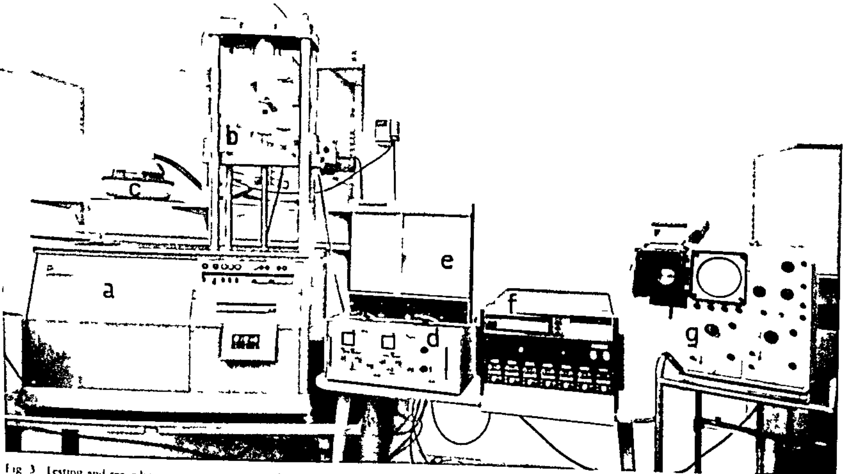


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butterfly screw on the side (Fig 5) The samples were examined with the dissec tion microscope both while they were being loaded and also after loading The analysis of the load,deformation curves did not show any slipping of the samples and loading of the samples to the point of rupture resulted in the rupture of the ligaments in the free space between the clamps

METHODS OF TESTING

We carried out the following investigations in order to describe the tensile characteristics of the longitudinal ligaments

a) Determination of the breaking point of egments of ligaments of full dimension as well as samples of identical size
b) Repetitive loading of samples of identical size
c) The determination of the preloading point
d) Determination of the elastic properties of the ligament and their relation ship to deformation changes in the lumbar spine the level from which the ligament was taken and the age

Experiments in which the samples were exposed to room air were carried out at a temperature between 19—24°C and at a relative humidity between 60—70 per cent The studies in the high humidity chamber were performed in saturated air at 23—28°C

In the determination of the preloading point specimens were loaded at a rate of 0 5 to 50 mm/min in the range 10—1000 gm.

In the load tests carried out with the samples of identical size we loaded and unloaded the samples successively with 500 gm at 35 second intervals We obtained three significantly differing curves (see page 40) In the studies designed to determine the elastic properties of the ligaments in relation to degenerative changes and age the samples were placed in a high humidity chamber and loaded to 500 gm After one minute we measured the stress relaxation i e the decrease in stress at a constant deformation Then after waiting a further three minutes we loaded the sample again After a certain amount of time which was arbitrarily chosen to be one minute the sample was loaded again then immediately unloaded and in this way we obtained curves which showed very small residual deformation The determination was repeated once more to see whether the curves were repeatable and whether all the parameters of the curve were identical In order to determine whether one could rely on the results obtained from the sample we carried out the same test on one or two more samples taken from the same segment of the ligament. The results were compared and if the curves did not correlate this particular study of the test sampl was discarded and not included for analysis in our material

HIGH HUMIDITY CHAMBER

After preliminary tests on ligaments exposed to air we decided that, in order to minimize the water loss which affects the physical properties of the tissue it would be necessary to provide a high humidity environment Thus we had a special humidity chamber constructed out of Plexiglass which surrounded that part of the testing machine in which the test sample was placed This humidity chamber was connected to a 'Defensor humidifier which can produce 80 m³ of saturated air per hour This machine raises the relative humidity in the chamber to 100 per cent within 5 minutes The humidity as well as the temperature of the air within the chamber was measured at the level of the test sample with a hygrometer and a thermometer Although condensation can sometimes be observed on the chamber walls experiments (see page 36) have shown that this does not result in up take of water by the sample A second high humidity chamber which was equipped with a high output humidifier (Defensor) was used during the preparation of samples The front wall of this chamber was made of glass and this allowed us to prepare the ligaments under visual control with an environ mental humidity of 100 per cent The humidity was measured with a hygrometer (Inor) which was suspended at the level of the preparations During the transfer of the ligaments from the high humidity chamber to the microtome and from the microtome to the testing machine the ligaments were wrapped in a polyethylene sheet

CLAMPS

Ligaments have a tendency to slip out of clamps and thus it was necessary to investigate different clamping procedures After carrying out experiments with a number of clamps we finally adopted a clamp which is closed by means of a

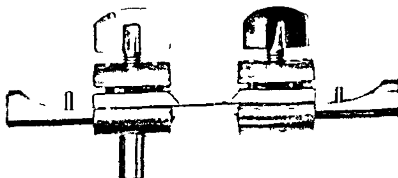


Fig 5 The test clamps

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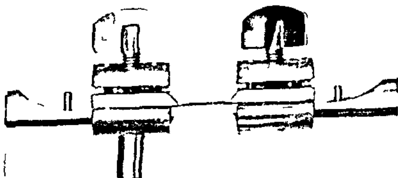


Fig 5 The test clamps

and ageing we employed punch cards On these cards we recorded the results obtained from our curves radiological examinations as well as histological studies of the disc and of the ligaments before and after loading

Statistical methods

The statistical methods employed in this work are the following

1 In studying samples exposed to air and samples placed in different solutions sign tests have been performed

2 In comparing samples from anterior and posterior ligaments and in comparing samples from degenerated and non degenerated specimens Students t test has been applied to the differences between measurements from samples that have been considered as paired This technique has also been employed in the comparison between frozen and control samples and in comparing the sample weights before and after placing th m in a high humidity chamber

3 In order to investigate the influence of age and level regression equations have been fitted to the data by means of the method of least squares

4 Graphical illustrations in air exposure experiments and swelling curves are fitted to the computed means but the age dependence graphs are products of the method of least squares

The sign test and t test when applied to differences both serve as tools to test whether there are different means in two groups or not Both methods require every observation in one group to be matched to an observation in the other group

In the air exposure and swelling experiments the observations in the two groups are actually from the same samples before and after treatment and clearly paired In the other comparisons observations have been considered paired The *t test* performed on differences from such pairs then shows whether the mean difference should be considered as zero

The sign test does not take into account the value of the difference but only its sign Under the necessary assumption *of differences* being normally distributed the t test always shows a significant difference between group means if a sign test does (the converse not being true) Consequently when a sign test showed a significant difference the more involved computation work of the t test was not performed

The method of least squares is the method of fitting a line to given data so as to minimize the sum of squared deviations *from this line* e g assuming a model

$$Y = C_0 + C_1 X_1 + C_n X_n +$$

determine the coefficients C_0 C_1 C

EVALUATION OF THE CURVES

The following parameters were evaluated from the load/deformation curves

The total deformation during loading the residual deformation in the sample and the energy dissipation The deformation was calculated from the curve on the basis of simple measurement and expressed in mm Energy dissipation was calculated with the aid of a planimeter (Amsler accuracy of 1/10th cm²) from the area contained between the loading and the unloading curve The resulting energy loss is calculated in gm mm The failure load of the samples was measured from the graphs and expressed in Kg

HISTOLOGICAL STUDIES

Histological studies were carried out on longitudinal and transverse sections of the anterior and posterior portions of the annulus fibrosus Sections of the anterior and posterior longitudinal ligaments were obtained at the disc level as well as at the level of the vertebral bodies In order to prevent buckling of the ligaments on removal from the spine they were fastened to a rigid base Ligaments which were previously tested by loading were similarly fastened and fixed in 10 per cent formalin After fixation the disc material as well as the sections from the ligaments were treated by standard histological methods and stained with Eosin and hematoxyline In those experiments in which we studied the behaviour of collagen bundles under the influence of different loads we used very thin sections of unstained tissue These ligaments were stretched under the microscope by means of special clamps which were loaded with weights varying from 10—100 gm In subsequent experiments ligaments were stretched in the Alwetron machine to a predetermined load and then compressed between two glass plates before being photographed under the microscope

RADIOLOGICAL EXAMINATIONS

All lumbar spines obtained were X rayed in both the anteroposterior and lateral projections The roentgenograms so obtained were analyzed and graded according to the degeneration For this analysis the disc height and lipping were taken as criteria Occasionally we found spina bifida spondylosis and old fractures in the vertebral bodies The radiological grading was subsequently correlated with the results obtained by histological methods

COLLECTION AND RECORDING OF DATA

All experimental data were tabulated and subsequently analyzed statistically employing standard statistical methods Where data were being collected in order to determine the correlation between the elasticity and the degenerative changes

V DISCUSSION OF METHODS

Water loss of samples exposed to air

In our initial investigations of the tensile properties of the longitudinal ligaments of the lumbar spine we observed that the physical properties of these ligaments could change rapidly with dehydration. When we introduced samples of small dimensions (1 mm² in cross section) this led to an even more rapid change in their physical properties as the rate of water loss was greater. We observed that samples exposed to air for 8 minutes gave different curves from those obtained with fresh tissue. In order to determine the rate and the amount of water loss we carried out the following experiment.

From two lumbar spines (nos. 1, 2, Table I) which were in a high humidity chamber we obtained 14 samples of the following dimensions: 20×2×0.5 mm. Each sample was immediately enveloped tightly in polyethylene and stored in this fashion until it was weighed. The samples were weighed on a precision balance (E. Mettler type H 16). These were subsequently exposed to air. During the exposure the relative humidity was 60—70 per cent and the air temperature 20°C. Six samples were weighed at 3 minute intervals during a period of 30 minutes (Table III). Eight samples were weighed at 5, 10 and 30 minutes after initial exposure (Table IV).

Results

TABLE III

Series of 6 samples

Minutes	0	3	6	9	12	15
Mean weight (gm) Standard deviation	0.0446 0.0010	0.0437 0.0014	0.0421 0.0015	0.0408 0.0015	0.0396 0.0018	0.0388 0.0014

Minute	18	21	24	27	30	
Mean weight (gm) Standard deviation	0.0375 0.0013	0.0367 0.0013	0.0359 0.0014	0.0350 0.0015	0.0341 0.0016	

TABLE IV

Series of 8 samples

Minutes	0	5	10	30
Mean weight (gm) Standard deviation	0.0424 0.0010	0.0388 0.0016	0.0369 0.0012	0.0320 0.0012

so that the sum of all squared deviations

$$(Y-C_0-C_1X_1-C_2X_2- \qquad)^2$$

has a minimum value

To test whether the coefficients differ significantly from zero or not t tests are carried out

All computation work involving the 'method of least squares has been performed in a computer

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Minutes	0	3	6	9	12	15
Mean weight (gm) St dard de iation	0 0446 0 0010	0 0432 0 0014	0 0421 0 0015	0 0408 0 0015	0 0396 0 0018	0 0388 0 0014

Minutes	18	21	24	27	30	
Mean w ght (gm) St ndard d t n	0 0375 0 0013	0 0367 0 0013	0 0359 0 0014	0 03 0 0 0015	0 0341 0 0016	

TABLE IV

Ser f 8 s mpl

Min ces	0	5	10	30
Mean we ght (gm) Standard deviation	0 0474 0 0010	0 0388 0 0016	0 0369 0 0012	0 0370 0 0012

To test the hypothesis that there is no effect of exposing the samples to air a *sign test* was performed This was applied on the initial weight and on the first weight after exposure to air

Since every sample in both series has decreased in weight the hypothesis of no effect is rejected in both cases Water loss of samples is presented graphically (Fig 6)

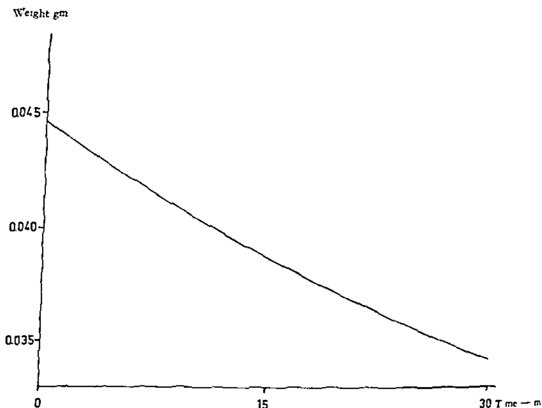


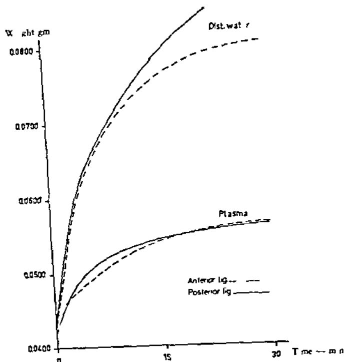
Fig 6 Loss of weight of samples in air at 64 per cent relative humidity and 20°C temperature

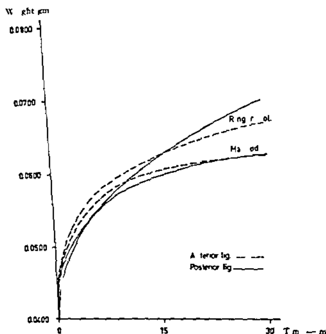
CONCLUSION

The drying of small samples which we employed in the testing of the tensile properties of ligaments takes place very rapidly During the test procedure prolonged exposure to air at 60—70 per cent relative humidity and 20 C temperature led to a much more significant water loss from the samples

BEHAVIOUR OF THE ANTERIOR AND POSTERIOR LONGITUDINAL LIGAMENTS IN DIFFERENT SOLUTIONS

In order to find out if the water loss from the samples could be prevented by means of immersion in different solutions such as distilled water Ringer solution *human plasma and Macrodex* we carried out the following experiments





F g 7 Swelling curves of samples of anterior and posterior longitudinal ligaments in different solutions.

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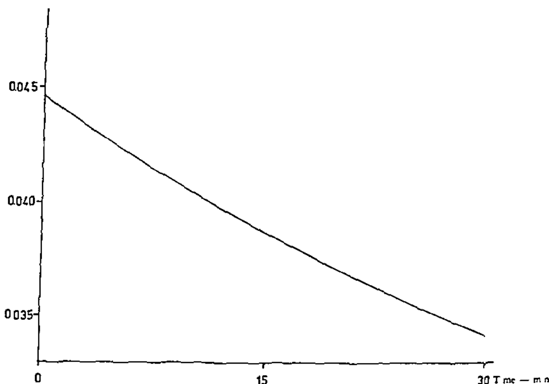


Fig 6 Loss of weight of samples in air at 64 per cent relative humidity and 20°C temperature

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Plasma

ant.	440	14	462	13	472	12	505	13	516	12	557	19
post.	413	11	460	12	489	12	511	15	519	12	558	12

Macrodex

ant.	430	15	504	15	530	19	553	17	569	16	619	16
post	410	11	474	17	518	17	553	23	563	23	621	27

To test whether there is a significant difference between mean weight at the beginning of the experiment and after three minutes in a particular solution a sign test has been performed

Since every sample in every experiment has increased in weight the sign test shows a significant difference between the weight of the sample before and after placing in the solution

CONCLUSION

There was no difference between the fluid uptake of samples obtained from the anterior longitudinal ligament and from the posterior longitudinal ligament. A significant increase in the weight of the samples takes place after three minutes of immersion in distilled water Ringer solution human plasma or Macrodex.

Distilled water was most rapidly taken up by the samples human plasma and Macrodex showed the lowest uptake (see Fig 7) The fluid uptake was so rapid and so great that storage of ligament samples by wrapping them in gauze previously soaked in some solution could not be employed.

Water loss from samples in the high humidity chamber

The experiments which were carried out in order to determine the water loss from samples exposed to air (at 60—70 per cent relative humidy and 20—24°C) as well as the experiments on the solution uptake of samples led to the conclusion that environmental conditions must be created which would lead to the following

1 No water loss from the sample during the test procedure

2 No fluid uptake of the sample during the test procedure.

Such environmental conditions can be created if the test is carried out in air which is saturated with water vapour In order to prove that such environmental conditions existed in a high humidity chamber and thus would meet our two test requirements the following experiment was carried out.

From two lumbar spine (Table I nos 3 4) ten samples were obtained from the anterior longitudinal ligament and ten from the posterior longitudinal ligament.

We obtained 48 samples of dimension 20×2×0 5 mm from four lumbar spines (nos 5, 6 7, 8, Table I) The samples were divided into two groups of 24 one group consisting of samples taken from the anterior longitudinal ligament and the second group of samples consisting of those taken from the posterior longitudinal ligament In order to have objective results and not rely on data obtained from one lumbar spine, we then mixed the samples (within the groups anterior and posterior) and divided them into eight groups of six This gave us four groups each consisting of six samples from the anterior longitudinal ligament and four groups consisting of six of the posterior longitudinal ligament These units of six we shall refer to as sub-groups Each sub-group was then tested in the following solutions Ringer solution human plasma Macrodex and distilled water The experiment was carried out separately on the sub-groups comprising the anterior longitudinal ligament and those comprising the posterior longitudinal ligament A sample after it was removed from the solution was placed between two sheets of Munktell filter paper no 3 for five seconds in order to remove the superficial solution and these were subsequently weighed at intervals of 3 6 9 12 30 and 60 minutes Immediately after weighing the samples were reimmersed in their respective solutions The results obtained after three minutes of immersion were analyzed statistically and compared with the initial weight A graphical correlation was also carried out between the results obtained in samples from the anterior longitudinal ligament and the posterior longitudinal ligament The fluid uptake of the samples was plotted on a graph which gave us *swelling curves* (*Fig* 7)

Results

TABLE V

Means (M) and Standard deviations (S D) for samples in different solutions

All figures computed from data of six samples and expressed in gm

All figures are to be multiplied by 10^{-4}

Water

	0 min		3 min		6 min		9 min		12 min		30 min	
	M	S D	M	S D	M	S D	M	S D	M	S D	M	S D
ant	428	12	499	17	602	30	645	32	693	27	803	24
post	432	7	524	17	619	17	657	16	68[illegible]	13	886	[illegible]

Ringer

ant	433	13	514	18	540	15	569	17	578	17	658	21
post	418	13	498	12	518	13	549	15	563	17	685	17

(along the longitudinal axis) into two halves One half was kept in a high humidity chamber whilst the other half was immediately transferred to the Cryo microtome where it was frozen to —60 C with carbon dioxide snow Subsequently it was taken back to the high humidity chamber and allowed to thaw The thickness of the corresponding halves was then measured Once it was established that both halves had the same thickness we obtained two samples from each half In this way we had two samples from both the frozen and control halves of the anterior longitudinal ligamen s at the levels of L5 L4 L3 and L2 From the posterior longitudinal ligaments we were able to get only four samples two from the level of L3 and two from L4 respectively as the other levels were not wide enough to allow for sampling Samples thus obtained were then mechanically tested in a high humidity chamber and the resulting data were compared The parameters of the load deformation curves from corresponding levels of the lumbar spine were very similar The curves differed systematically and this was related to the difference in the thickness of the ligament at the different levels of the lumbar spine

TABLE VI

(Figu es a e shown ± S D)

	before freezing	after freezing	n	t
Elongation mm	0 59 ± 0 037	0 59 ± 0 037	20	0 68
Residual d formation mm	0 16 ± 0 033	0 16 ± 0 43	20	0 57
Energy d ss pation gm mm	4 18 ± 0 51	4 17 ± 0 49	20	1 0

CONCLUSION

Rapid freezing of the ligaments to —60°C with subsequent thawing does not influence the tensile property of these ligaments

Experiment 2

Using our routine method we prepared six samples from both the anterior and posterior ligaments of a lumbar spine (Table I no 11) The samples were then tested In this way we got repeatable curves Subsequently without removing the sample from the clamps it was frozen with the dioxide snow and immediately thawed (the whole manoeuvre took about *three minutes* to carry out) The sample together with the clamps was then reinserted in the test machine and two successive loadings were carried out The curves thus obtained did not differ from the previous curves

CONCLUSION

Rapid freezing of ligaments to a temperature of —60°C and subsequent thawing does not influence their tensile properties

After complete mixing ten of these were placed in the high humidity test chamber and ten in the high humidity preparation chamber The humidity in these chambers was continuously monitored during these experiments and the environment immediately surrounding the sample was maintained at 100 per cent relative humidity In the test chamber the temperature was 26°C and in the preparation chamber 24°C The samples were maintained in each chamber for a period of one hour After 10 minutes in the test chamber we noticed considerable condensation occurring on the walls of the chamber We thought that similar condensation could be occurring on the samples which might lead to a subsequent uptake of water In order to check whether this phenomenon was taking place as well as to determine whether any water loss occurred while the samples were in the humidity chamber all samples were removed after one hour and immediately weighed

RESULTS

For each sample the weights before and after the experiment were determined *and the results were analyzed by means of a t test*

For the 20 differences it was found that

Mean difference = 0 000015

Standard deviation of differences = 0 000080

This yields a t value of 0 83 which is obviously not significant

CONCLUSION

In a high humidity chamber containing air of 100 per cent relative humidity at a temperature of approximately 25°C both water loss and water uptake by the sample can be prevented The condensation on the walls of the chamber did not lead to a similar condensation on the sample

Influence of rapid freezing and thawing on the tensile properties of the ligaments

In order to obtain sheets of uniform thickness our material was frozen at a temperature of —60°C As we felt that this sudden freezing and thawing might influence the physical properties of the *longitudinal ligaments* we performed the following experiments

Experiment 1

The anterior and posterior longitudinal ligaments of two lumbar spines (Table I nos 9 10) were prepared in a high humidity chamber These were then divided into segments corresponding to lumbar levels Each sample was carefully divided

(along the longitudinal axis) into two halves One half was kept in a high humidity chamber whilst the other half was immediately transferred to the Cryo microtome where it was frozen to —60°C with carbon dioxide snow Subsequently it was taken back to the high humidity chamber and allowed to thaw The thickness of the corresponding halves was then measured Once it was established that both halves had the same thickness we obtained two samples from each half In this way we had two samples from both the frozen and control halves of the anterior longitudinal ligaments at the levels of L5 L4 L3 and L2 From the posterior longitudinal ligaments we were able to get only four samples two from the level of L3 and two from L4 respectively as the other levels were not wide enough to allow for sampling Samples thus obtained were then mechanically tested in a high humidity chamber and the resulting data were compared The parameters of the load deformation curves from corresponding levels of the lumbar spine were very similar The curves differed systematically and this was related to the difference in the thickness of the ligament at the different levels of the lumbar spine

TABLE VI

(Figu s a shown ± S D)

	before freezing	after freezing	n	t
Elongation mm	0 59 ± 0 037	0.59 ± 0 037	20	0 68
Residual deformation mm	0 16 ± 0 033	0 16 ± 0 43	20	0.57
Energy dissipation gm. mm	4 18 ± 0.51	4 17 ± 0 49	20	1 0

CONCLUSION

Rapid freezing of the ligaments to —60°C with subsequent thawing does not influence the tensile property of these ligaments

Experiment 2

Using our routine method we prepared six samples from both the anterior and posterior ligaments of a lumbar spine (Table I no 11) The samples were then tested In this way we got repeatable curves Subsequently without removing the sample from the clamps it was frozen with the dioxide snow and immediately thawed (the whole manoeuvre took about three minutes to carry out) The sample together with the clamps was then reinserted in the test machine and two successive loadings were carried out The curves thus obtained did not differ from the previous curves

CONCLUSION

Rapid freezing of ligaments to a temperature of —60 C and subsequent thawing does not influence their tensile properties

After complete mixing ten of these were placed in the high humidity test chamber and ten in the high humidity preparation chamber The humidity in these chambers was continuously monitored during these experiments and the environment immediately surrounding the sample was maintained at 100 per cent relative humidity In the test chamber the temperature was 26°C and in the preparation chamber, 24°C The samples were maintained in each chamber for a period of one hour After 10 minutes in the test chamber we noticed considerable condensation occurring on the walls of the chamber We thought that similar condensation could be occurring on the samples which might lead to a subsequent uptake of water In order to check whether this phenomenon was taking place as well as to determine whether any water loss occurred while the samples were in the humidity chamber all samples were removed after one hour and immediately weighed

RESULTS

For each sample the weights before and after the experiment were determined and the results were analyzed by means of a t test

For the 20 differences it was found that

Mean difference = 0 000015

Standard deviation of differences = 0 000080

This yields a t value of 0 83 which is obviously not significant

CONCLUSION

In a high humidity chamber containing air of 100 per cent relative humidity at a temperature of approximately 25°C both water loss and water uptake by the sample can be prevented The condensation on the walls of the chamber did not lead to a similar condensation on the sample

Influence of rapid freezing and thawing on the tensile properties of the ligaments

In order to obtain sheets of uniform thickness our material was frozen at a temperature of —60°C As we felt that this sudden freezing and thawing might influence the physical properties of the longitudinal ligaments we performed the following experiments

Experiment 1

The anterior and posterior longitudinal ligaments of two lumbar spines (Table I nos 9 10) were prepared in a high humidity chamber These were then divided into segments corresponding to lumbar levels Each sample was carefully divided

(along the longitudinal axis) into two halves One half was kept in a high humidity chamber whilst the other half was immediately transferred to the Cryo microtome where it was frozen to —60°C with carbon dioxide snow Subsequently it was taken back to the high humidity chamber and allowed to thaw The thickness of the corresponding halves was then measured Once it was established that both halves had the same thickness we obtained two samples from each half In this way we had two samples from both the frozen and control halves of the anterior longitudinal ligaments at the levels of L5 L4 L3 and L2 From the posterior longitudinal ligaments we were able to get only four samples two from the level of L3 and two from L4 respectively as the other levels were not wide enough to allow for sampling Samples thus obtained were then mechanically tested in a high humidity chamber and the resulting data were compared The parameters of the load/deformation curves from corresponding levels of the lumbar spine were very similar The curves differed systematically and this was related to the difference in the thickness of the ligament at the different levels of the lumbar spine

TABLE VI

(Figures are shown ± S D)

	before freezing	after freezing	n	t
Elongation mm	0 59 ± 0 037	0 59 ± 0 037	20	0 68
Residual deformation mm	0 16 ± 0 033	0 16 ± 0 43	20	0.57
Energy dissipation gm. mm	4 18 ± 0 51	4 17 ± 0 49	20	1 0

CONCLUSION

Rapid freezing of the ligaments to —60°C with subsequent thawing does not influence the tensile property of these ligaments

Experiment 2

Using our routine method we prepared six samples from both the anterior and posterior ligaments of a lumbar spine (Table I to II) The samples were then tested In this way we got repeatable curves Subsequently without removing the sample from the clamps it was frozen with the dioxide snow and immediately thawed (the whole manoeuvre took about three minutes to carry out) The sample together with the clamps was then reinserted in the test machine and two successive loadings were carried out The curves thus obtained did not differ from the previous curves

CONCLUSION

Rapid freezing of ligaments to a temperature of —60 C and subsequent thawing does not influence their tensile properties

After complete mixing ten of these were placed in the high humidity test chamber and ten in the high humidity preparation chamber The humidity in these chambers was continuously monitored during these experiments and the environment immediately surrounding the sample was maintained at 100 per cent relative humidity In the test chamber the temperature was 26°C and in the preparation chamber 24°C The samples were maintained in each chamber for a period of one hour After 10 minutes in the test chamber we noticed considerable condensation occurring on the walls of the chamber We thought that similar condensation could be occurring on the samples which might lead to a subsequent uptake of water In order to check whether this phenomenon was taking place as well as to determine whether any water loss occurred while the samples were in the humidity chamber all samples were removed after one hour and immediately weighed

RESULTS

For each sample the weights before and after the experiment were determined and the results were analyzed by means of a t test

For the 20 differences it was found that

Mean difference = 0 000015

Standard deviation of differences = 0 000080

This yields a t value of 0 83 which is obviously not significant

CONCLUSION

In a high humidity chamber containing air of 100 per cent relative humidity at a temperature of approximately 25°C both water loss and water uptake by the sample can be prevented The condensation on the walls of the chamber did not lead to a similar condensation on the sample

Influence of rapid freezing and thawing on the tensile properties of the ligaments

In order to obtain sheets of uniform thickness our material was frozen at a temperature of —60°C As we felt that this sudden freezing and thawing might influence the physical properties of the longitudinal ligaments we performed the following experiments

Experiment 1

The anterior and posterior longitudinal ligaments of two lumbar spines (Table I nos 9 10) were prepared in a high humidity chamber These were then divided into segments corresponding to lumbar levels Each sample was carefully divided

Studies on the loading capacity of samples of equal dimensions

From three lumbar spines (Table I nos 66 73 74) we obtained samples of standard dimensions The samples were wider at their ends (dumb-bell shaped) to facilitate their insertion into the clamps The significant dimensions were thickness (0 5 mm) and width (2 mm) at the mid section The distance between the clamps was always 9 mm. The samples were subsequently loaded to failure Of 30 studies 26 were suitable for analysis (see Table VIII) The remainder either because of slippage from the clamps or tearing at the clamps were considered unsuitable for analysis and were rejected These experiments were carried out in order to assess the load level to be used in our subsequent experiments on the elastic properties of the ligaments

TABLE VIII

Number of specimen (Table I)	Age Years	Level	Lig ant		Lig post.	
			Yield kg	Failure load kg	Yield kg	Failure load kg
66	55	L[illegible]disc	1 6	1 9	1 6	2.1
66	55	L3	1 7	2.1	2 1	2.2
66	55	L4	1 7	2 3	1 8	1 9
66	55	L5	2 1	2.3	2 0	1 8
			1 77	2 15	1 87	2.0
74	64	L1	1 7	1 8	1 6	1 7
74	64	L2disc	1 9	2.1	1 9	1 9
4	64	L4	1 7	1 8	1 7	1 8
74	64	L5	1 8	1 9	1 8	1 9
			1 77	1 90	1 75	1 83
73	26	L1	1 7	2 1	1 6	2.0
3	2[illegible]	L[illegible]disc	1 8	2.0	1 7	1 9
73	[illegible]	L3	1 8	2.3	1 9	2.1
3	[illegible]	L4	2.0	2.5	1 8	2.3
73	26	L5	1 9	2.6	2.1	2.3
			1 84	2.30	1.82	2.12
Sample average			1 79	2.12	1.81	1 98

VI TENSILE CHARACTERISTICS OF LONGITUDINAL LIGAMENTS

Studies on the loading capacity of ligaments of full dimensions

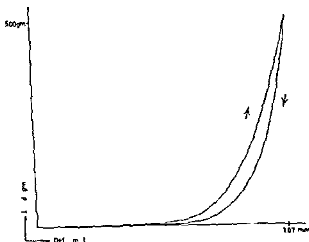
From three lumbar spines (Table I nos 67, 68, 72) the longitudinal ligaments were obtained The ligaments were then divided into segments corresponding to the vertebral body or disc levels These samples were then studied to determine their loading capacity The clamps were so adjusted that the distance between them was 10 mm The ligaments were loaded until they tore and a continuous record was made using a Philips XY recorder Although 22 segments of ligaments were tested only 14 were suitable for analysis The remainder had to be rejected because the ligaments slipped out of the clamps or tore at the point where they were held in the clamps The results are shown in table VII

TABLE VII

No of specimen (Table I)	Age Years	Level	Anterior ligament		Posterior ligament	
			Yield load Kg	Failure load Kg	Yield load Kg	Failure load Kg
67	36	L5	50	64	15 5	16
67	36	L4 disc	23	23	–	–
67	36	L3 disc	–	–	10	11
68	36	L5	46	54	–	–
68	36	L4 disc	15	22	18	20
68	36	L3	–	–	22	25
72	58	L5	20	32	20	22
72	58	L4 disc	10	20	15 5	16
72	58	L3 disc	18	21	14	17

CONCLUSION

Because of the difference in the dimensions of the ligaments we obtained results which differed greatly We could assume that the anterior and posterior longitudinal ligaments are slightly weaker at the level of the disc. It also appears that there is a greater difference between the yield point and the failure point for the anterior longitudinal ligament than for the posterior longitudinal ligament The posterior longitudinal ligament ruptures almost immediately after the yield point



c) Third cycle

old spines The failure loads for a young spine (26 years) were 2 30 Kg for the anterior ligament and 2 12 Kg for the posterior ligament whereas for an old spine (64 years) the corresponding values were 1 90 Kg and 1 83 Kg respectively There is no difference between the loading capacity of samples taken from the body and disc levels

Load tests repeated at 35 second intervals

It is generally known that repeated loading of ligaments tendons or segments of the annulus fibrosus produces with each repeated loading a more elastic response (Virgin 1951 Rigby 1964 Rolander 1966 Viidik 1966 Galante 1967) In order to determine the effect of repeated loading on the ligaments all samples were cyclically loaded three times between 0 and 500 gm at 35 second intervals For these determinations a total of 50 samples of the anterior longitudinal ligament and 55 samples of the posterior longitudinal ligament were prepared from spines nos 13— 33 Table I

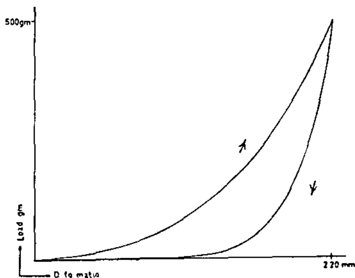
RESULTS

The results show that there was a great difference between the curves obtained from each of the three load cycles (Fig 8 a b c) Both the residual deformation and maximum deformation were seen to decrease with each successive load cycle In order to assist comparison we have forced the mean values of the parameters obtained during the third load cycle to be unity and the following data have resulted

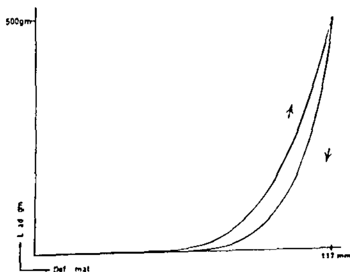
CONCLUSION

The average failure load of standard samples of the anterior longitudinal ligaments was 2 12 Kg and of the posterior longitudinal ligaments 1 98 Kg The lowest failure load for the anterior longitudinal ligament was 1 8 Kg and for the posterior 1 7 Kg From this we concluded that for subsequent experiments a loading of 0 5 Kg should be used which represented about 30 per cent of the failure load of the weakest sample used in the previous analysis and only 25 per cent of the average failure load of both the anterior and posterior longitudinal ligaments There was an obvious difference between specimens from young and

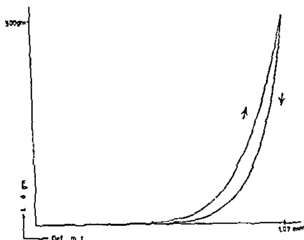
Fig 8 Load cycling Sample load/deformation curves obtained at 35-second intervals



a) First cycle



b) Second cycle



c) Thi d cycle

old spines The failure loads for a young spine (26 years) were 2 30 Kg for the arterior ligament and 2 12 Kg for the posterior ligament, whereas for an old spine (64 years) the corresponding values were 1 90 Kg and 1 83 Kg respec tively There is no difference between the loading capacity of samples taken from the body and disc levels

Load tests repeated at 35 second intervals

It is generally known that repeated loading of ligaments tendons or segments of the annulus fibrosus produces with each repeated loading a more elastic response (Virgin 1951 Rigby 1964 Rolander 1966 Viidik 1966 Galante 1967) In order to determine the effect of repeated loading on the ligaments all samples were cyclically loaded three times between 0 and 500 gm at 35 second intervals For these determinations a total of 50 samples of the anterior longitudinal ligament and 55 samples of the posterior longitudinal ligament were prepared from spines nos 13—33 Table I

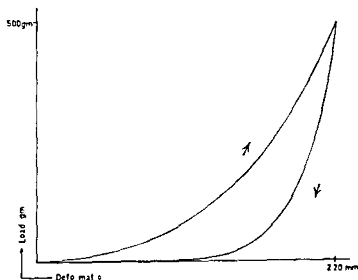
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The results show that there was a great difference between the curves obtained from each of the three load cycles (Fig 8 a, b c) Bo h the residual deformation and maximum deformation were seen to decrease with each successive load cycle In order to assist comparison we have for ed the mean values of the parameters obtained during the third load cycle to be unity and the following data have resulted

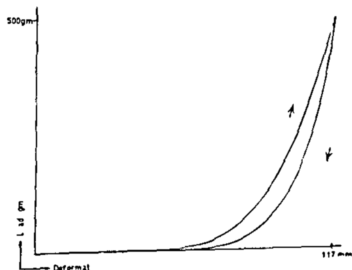
CONCLUSION

The average failure load of standard samples of the anterior longitudinal ligaments was 2.12 Kg and, of the posterior longitudinal ligaments 1.98 Kg. The lowest failure load for the anterior longitudinal ligament was 1.8 Kg and for the posterior 1.7 Kg. From this we concluded that for subsequent experiments a loading of 0.5 Kg should be used which represented about 30 per cent of the failure load of the weakest sample used in the previous analysis and only 25 per cent of the average failure load of both the anterior and posterior longitudinal ligaments. There was an obvious difference between specimens from young and

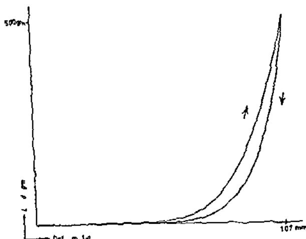
Fig. 8. Load cycling. Sample load/deformation curves obtained at 35-second intervals.



a) First cycle



b) Second cycle



c) Third cycle

old spines The failure loads for a young spine (26 years) were 2 30 Kg for the anterior ligament and 2 12 Kg for the posterior ligament whereas for an old spine (64 years) the corresponding values were 1 90 Kg and 1 83 Kg respectively There is no difference between the loading capacity of samples taken from the body and disc levels

Load tests repeated at 35 second intervals

It is generally known that repeated loading of ligaments tendons or segments of the annulus fibrosus produces with each repeated loading a more elastic response (Virgin 1951 Rigby 1964 Rolander 1966 Viidik 1966 Galante 1967) In order to determine the effect of repeated loading on the *ligaments all* samples were cyclically loaded three times between 0 and 500 gm at 35 second intervals For these determinations a total of 50 *samples of the* anterior longitudinal ligament and 55 samples of the posterior longitudinal ligament were prepared from spines nos 13—33 Table I

RESULTS

The results show that there was a great difference between the curves obtained from each of the three load cycles *(Fig 8 a b c) Both* the residual deformation and maximum deformation were seen to decrease with each successive load cycle In order to assist comparison we have *forced* the mean values of the parameters obtained during the third load cycle to be unity and the following data have resulted

TABLE IX

Comparison between mean parameters (105 samples)

	1st load cycle	2nd load cycle	3rd load cycle
Deformation			
Anterior	1 865	1 113	1 00
Posterior	1 815	1 107	1 00
Residual deformation			
Anterior	3 501	1 264	1 00
Posterior	3 864	1 242	1 00
Energy dissipation			
Anterior	2 766	1 199	1 00
Posterior	2 824	1 207	1 00

To compare the tensile properties of samples from anterior and posterior ligaments the following analysis was carried out 20 pairs of ligaments were tested each pair comprising a sample from the posterior and anterior ligaments of the same segment The differences betweeen measurements from anterior and posterior samples were calculated These differences were analyzed by means of a t test to investigate whether the mean difference could be considered as zero Such a comparison has been made for maximum deformation residual deformation and energy dissipation for each of the three load cycles

TABLE X

Deformation (mm)

	1st load cycle	2nd load cycle	3rd load cycle
Mean difference between lig ant. and post (paired observ)	0 1640	0 0105	0 0490
Standard error of differences	0 25	0 17	0 18
Computed t value	2 67	0.24	1 01

TABLE XI

Residual deformation (mm)

	1st load cycle	2nd load cycle	3rd load cycle
Mean difference between lig ant. and post (paired observ)	0 1495	0 0815	0 0590
Standard error of differences	0 27	0 09	0 06
Computed t value	2.23	3.39	2.96

TABLE XII

Energy dissipation (gm mm)

	1st load cycle	2nd load cycle	3rd load cycle
Mean difference between lig ant and post (paired observ)	2.1650	0 9700	0 9300
Standard error of differences	3 7	2 0	1 4
Computed t value	2 40	1 88	2.40

CONCLUSION

The results show that there are significant differences between the parameters obtained from the anterior and posterior longitudinal ligaments although these differences decrease in the second and third load cycles

Comparing the mean parameters of each load cycle for the anterior and posterior ligaments showed that there was a similar proportional change between cycles

VII STUDIES TO OBTAIN THE PRELOADING POINT FOR LONGITUDINAL LIGAMENTS OF THE LUMBAR SPINE

Investigation of shrinkage of the ligaments

The parameters which we obtained from repeated load tests led us to doubt if a material which exhibited such significant residual deformation and large energy dissipation could perform a physiological function For example a residual strain greater than 10 per cent would make the ligament mechanically useless in the living organism These results and the fact that the ligaments shrank on removal from the spine suggested that a more comprehensive study should be made A whole series of queries arises but the most obvious is the influence of *death on the mechanical properties of the ligaments At the moment this* question can only be answered hypothetically as we are in no position to prove our points However if we consider the ligament as a visco elastic substance and if we analyze it from a theoretical point of view then within the ligament there must exist a certain fluid pressure during life This pressure is maintained by means of a complex equilibration system with the pressure within the circulatory system The moment the heart stops beating and the circulatory pressure drops to zero the system reequilibrates and the internal pressure within the ligament may also drop thus affecting the mechanical properties of the tissue The fact that a ligament shrinks or shortens immediately after it is obtained from the lumbar spine indicates that this ligaments exists in a state of prestress To what extent the prestress of the ligament changes with death or preparation is difficult to assess however it is possible to estimate this prestress by performing experiments on fresh autopsy specimens

Experiment I

Ten randomly selected lumbar spines were tested in the following manner On the surface of the ligaments at different lumbar levels pairs of points were marked and the distance between each pair of points was then carefully measured In each *segment no attention* was paid to the position of the gauge length relative to the disc and vertebral body The ligaments were then removed from the lumbar spine and the separation of the previously marked points was again measured In every case *the ligaments shortened by a few mm*

Results See Table XIII

TABLE XIII

Amount of shrinkage

No	Lig	Age	Level	Dimension before shrinkage mm	Dimension after shrinkage mm	Shrinkage per cent	Average for each ligament	
							mm	per cent
1	Ant	64	L-5	30	28	6.7		
1		64	L-4	30	28	6.7		
1		64	L-3	30	27.5	8.3		
1		64	L-2	30	27	10.0	2.4	7.9
1	Post	64	L-5	30	28	6.7		
1		64	L-4	30	28	6.7		
1		64	L-2	30	27	10.0	2.3	7.8
2	Ant	25	L-5	20	17	15.0		
2		25	L-3	20	17	15.0		
2		25	L-2	20	18	10.0	2.7	13.3
2	Post	25	L-5	20	16	20.0		
2		25	L-3	20	16	20.0		
2		25	L-2	20	17	15.0	3.7	18.3
3	Ant	55	L-5	30	28	6.7		
3		55	L-4	30	28	6.7		
3		55	L-3	30	27.5	8.3		
3		55	L-2	30	27	10.0	2.4	7.9
3	Post	55	L-5	30	27	10.0		
3		55	L-4	30	27.5	8.3		
3		55	L-3	30	26	13.3		
3		55	L-2	30	27	10.0	3.1	10.4
4	Ant	17	L-4	30	27	10.0		
4		17	L-3	30	27	10.0		
4		17	L-2	30	26	13.3	3.3	11.1
4	Post	17	L-4	30	26	13.3		
4		17	L-3	30	6	13.3		
4		1	L-2	30	26	13.3	4.0	13.3
5	Ant	66	L-5	30	29	3.3		
5		66	L-4	30	28	6.7		
5		66	L-3	30	28	6.7		
5		66	L-2	30	27.5	8.3	1.9	6.3
5	Post	66	L-5	30	28	6.7		
5		66	L-4	30	28	6		
5		66	L-3	30	27	10.0		
5		66	L-2	30	27	10.0	2.5	8.4
6	Ant	58	L-5	30	27	10.0		
6		58	L-4	30	8	6.7		
6		58	L-3	30	28	6.7	2.3	7.8
6	Post	58	L-5	30	27	10.0		
6		58	L-4	30	26.5	11.7		
6		59	L-3	30	27	10.0		
6		58	L-2	30	[illegible]	10.0	3.1	10.4

VII STUDIES TO OBTAIN THE PRELOADING POINT FOR LONGITUDINAL LIGAMENTS OF THE LUMBAR SPINE

Investigation of shrinkage of the ligaments

The parameters which we obtained from repeated load tests led us to doubt if a material which exhibited such significant residual deformation and large energy dissipation could perform a physiological function For example a residual strain greater than 10 per cent would make the ligament mechanically useless in the living organism These results and the fact that the ligaments shrank on removal from the spine suggested that a more comprehensive study should be made A whole series of queries arises but the most obvious is the influence of death on the mechanical properties of the ligaments At the moment this question can only be answered hypothetically a we are in no position to prove our points However if we consider the ligament as a visco elastic substance and if we analyze it from a theoretical point of view then within the ligament there must exist a certain fluid pressure during life This pressure is maintained by means of a complex equilibration system with the pressure within the circulatory system The moment the heart stops beating and the circulatory pressure drops to zero the system reequilibrates and the internal pressure within the ligament may also drop thus affecting the mechanical properties of the tissue The fact that a ligament shrinks or shortens immediately after it is obtained from the lumbar spine indicates that this ligaments exists in a state of prestress To what extent the prestress of the ligament changes with death or preparation is difficult to assess however it is possible to estimate this prestress by performing experiments on fresh autopsy specimens

Experiment I

Ten randomly selected lumbar spines were tested in the following manner On the surface of the ligaments at different lumbar levels pairs of points were marked and the distance between each pair of points was then carefully measured In each segment no attention was paid to the position of the gauge length relative to the disc and vertebral body The ligaments were then removed from the lumbar spine and the separation of the previously marked points was again measured In every case the ligaments shortened by a few mm

Results See Table XIII

TABLE XIV

		Distance between wires		Contraction Per cent
		Before separation mm	After separation mm	
Spec No 47	Lig ant.	30	27	10
	Lig post.	30	26	13.3
Spec No 0	Lig ant	30	28	6 6
	Lig post.	30	27	10

CONCLUSION

The average amount of shrinkage obtained on sectioning *ligaments at the disc level in normal conditions* is the same as the shrinkage at the body vertebra level

Experiment 3

For this experiment lumbar spine no 73 (Table I) was used This lumbar spine showed no degenerative changes as determined by means of radiological technique and *microscopic* and macroscopic examinations A needle was inserted into the nucleus pulposus *between L3—L2 and L4—L3 levels* and *about* 0 3 cm^3 of water was injected into each Employing the intradiscal pressure measuring device of Nachemson it was *determined that the intradiscal pressure was raised by the injection of water from its resting pressure of 0 5 Kg/cm² to 7 Kg/cm²* at the level between L3—L2 and 5 Kg cm at the *level between L4—L3* Two points were marked on each ligament corresponding *to the discs* and vertebral bodies at the above mentioned levels The distance between these two points was then measured Subsequently the ligaments *were cut* and the distance between these points was again *measured*

Results See Table XV

No	Lig	Age	Level	Dimension before shrinkage mm	Dimension after shrinkage mm	Shrinkage per cent	Average for each ligament	
							mm	per cent
7	Ant	22	L-5	30	27	10 0		
7		22	L-4	30	27	10 0		
7		22	L 3	30	27	10 0		
7		22	L-2	30	28	6 7	2 8	9.2
7	Post.	22	L 5	30	26	13.3		
7		22	L-4	30	26	13 3		
7		22	L-3	30	26	13 3		
7		22	L-2	30	28	6 7	3 5	11 7
8	Ant	66	L-4	30	29	3.3		
8		66	L-3	30	28	6 7		
8		66	L 2	30	28	6 7	1 7	5 6
8	Post	66	L-4	30	28	6 7		
8		66	L-3	30	28	6 7		
8		66	L-2	30	27	10 0	2.3	7 8
9	Ant	4 5	L-5	20	17	15 0		
9		4 5	L-3	20	18	10 0	2 5	12 5
9	Post	4 5	L-5	20	17	15 0		
9		4 5	L-3	20	17	15 0	3 0	15 0
10	Ant	35	L-5	20	18	10 0		
10		35	L-3	20	18	10 0		
10		35	L 2	20	19	5 0	1 7	8 3
10	Post	35	L-5	30	28	6 7		
10		35	L-3	30	27	10 0		
10		35	L-2	30	27	10 0	2 7	8 9

Average shrinkage for young without degenerative changes lig ant 10 9%
lig post 13 1%
Average shrinkage for old with degenerative changes lig ant 7 1%
lig post 9 0%

Experiment 2

Two lumbar spines were used (nos 42 70 Table I) Two metal wires were inserted into both the anterior and posterior longitudinal ligaments in a direction perpendicular to the longitudinal axis of the fibres This was done at the disc level of L3—2 and L5—4 and the spines were then X rayed The ligaments were sectioned above and below the wires and with the spine and the X ray tube in the same relative position a second radiogram was made From the roentgenograms we obtained the changes in separation of the wires

Results See Table XIV

TABLE XIV

		Distance between wires		Contraction Per cent
		Before separation mm	After separation mm	
Spec. No 42	Lig ant	30	27	10
	Lig post.	30	26	13.3
Spec. No 70	Lig ant	30	28	6 6
	Lig post.	30	27	10

CONCLUSION

The average amount of shrinkage obtained on sectioning ligaments at the disc level in normal conditions is the same as the shrinkage at the body vertebra level

Experiment 3

For this experiment lumbar spine no 73 (Table I) was used This lumbar spine showed no degenerative changes as determined by means of radiological technique and microscopic and macroscopic examinations A needle was *inserted into the* nucleus pulposus between L3—L2 and L4—L3 levels and about 0 3 cm^3 of *water* was *injected* into each *Employing the intradiscal pressure measuring device of* Nachemson it was determined that the intradiscal pressure was raised by the injection of water from its resting pressure *of* 0 5 Kg/cm^2 *to* 7 Kg/cm at the level between L3—L2 and 5 Kg/cm at the level between L4—L3 Two points were marked on each ligament corresponding to the discs and vertebral bodies at the above mentioned levels The distance between these two points was then measured Subsequently the ligaments were cut and the distance between these points was again measured

Results See Table XV

No	Lig	Age	Level	Dimension before shrinkage mm	Dimension after shrinkage mm	Shrinkage per cent	Average for each ligament	
							mm	per cent
7	Ant.	22	L-5	30	27	10 0		
7		22	L-4	30	27	10 0		
7		22	L 3	30	27	10 0		
7		22	L-2	30	28	6 7	2.8	9.2
7	Post.	22	L 5	30	26	13.3		
7		22	L-4	30	26	13.3		
7		22	L-3	30	26	13 3		
7		22	L-2	30	28	6 7	3 5	11 7
8	Ant.	66	L-4	30	29	3.3		
8		66	L-3	30	28	6 7		
8		66	L 2	30	28	6 7	1 7	5 6
8	Post	66	L-4	30	28	6 7		
8		66	L 3	30	28	6 7		
8		66	L-2	30	27	10 0	2.3	7 8
9	Ant	4 5	L-5	20	17	15 0		
9		4 5	L-3	20	18	10 0	2.5	12.5
9	Post.	4 5	L-5	20	17	15 0		
9		4 5	L-3	20	17	15 0	3 0	15 0
10	Ant.	35	L 5	20	18	10 0		
10		35	L-3	20	18	10 0		
10		35	L 2	20	19	5 0	1 7	8.3
10	Post.	35	L-5	30	28	6 7		
10		35	L-3	30	27	10 0		
10		35	L-2	30	27	10 0	2.7	8 9

Average shrinkage for young without degenerative changes	lig ant.	10 9%
	lig post	13 4%
Average shrinkage for old with degenerative changes	lig ant	7 1%
	lig post.	9 0%

Experiment 2

Two lumbar spines were used (nos 42 70 Table I) Two metal wires were inserted into both the anterior and posterior longitudinal ligaments in a direction perpendicular to the longitudinal axis of the fibres This was done at the disc level of L3—2 and L5—4 and the spines were then X rayed The ligaments were sectioned above and below the wires and with the spine and the X ray tube in the same relative position, a second radiogram was made From the roentgenograms we obtained the changes in separation of the wires

Results See Table XIV

TABLE XIV

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For this experiment lumbar spine no 73 (Table I) was used This lumbar spine showed no degenerative changes as determined by means of radiological technique and microscopic and macroscopic examinations A needle was inserted into the nucleus pulposus between L3—L2 and L4—L3 levels and about 0 3 cm^3 of water was injected into each Employing the intradiscal pressure measuring device of Nachemson it was determined that the intradiscal pressure was raised by the injection of water from its resting pressure of 0 5 Kg/cm to 7 Kg/cm^2 at the level between L3—L2 and 5 Kg cm² at the level between L4—L3 Two points were marked on each ligament corresponding to the discs and vertebral bodies at the above mentioned levels The distance between these two points was then measured Subsequently the ligaments were cut and the distance between these points was again measured

Results See Table XV

TABLE XV

	Distance between points		Difference mm	Per cent
	Before cut mm	After cut mm		
Lig anterior				
L3 L2 disc level	23	16	7	30 4
L4-L3	20	15	5	25
L3 body vert level	25	20	5	20
Lig posterior				
L3 L2 disc level	20	10	10	50
L4-L3	20	12	8	40
L3 body vert level	25	15	10	40

In order to determine the shrinkage of ligaments from a segment of the lumbar spine where intradiscal pressure was not raised artificially the ligaments were cut in similar fashion at the levels of the S 1—L5 disc and L5 body vertebra

Results

TABLE XVI

	Distance between points		Difference mm	Per cent
	Before cut mm	After cut mm		
Lig anterior				
S1 L5 disc level	25	23	2	8
L5 body vert level	25	23	2	8
Lig posterior				
S1 L5 disc level	10	8 5	1 5	15
L5 body vert level	25	22	3	12

The shrinkage of the ligaments from segments of this vertebral column where the intradiscal pressure was not artificially raised did not differ from the shrinkage observed in the samples of ligaments studied from segments of other vertebral columns in previous experiments

CONCLUSION

Increase in the intradiscal pressure causes an increase in the prestress of the longitudinal ligaments of the vertebral column

Experiment 4

Specimen no 9 Table I

Using a thick needle and instruments used routinely for the extirpation of the nucleus pulposus the nuclei of the discs L4—L3 and L3—L2 were removed At a distance of 3 cm two points were marked on both the anterior and posterior longitudinal ligaments at the level of the L3 vertebral body In addition two points were marked at 2 cm separation on both ligaments between the levels of L4—L3 and L3—L2 The ligaments were then cut and the distance between the points was again measured

Results

TABLE XVII

	Distance between points		Difference mm	Per cent
	Before cut mm	After cut mm		
Lig anterior				
L3-L2 disc level	20	19	1	5
L4-L3	20	19 5	0.5	2.5
L3 body	20	19 5	0 5	2.5
Lig posterior				
L3-L2 disc level	20	18.5	1 5	7 5
L4 L3	20	19	1	5

On the level of S 1—L5 where the intradiscal pressure was not decreased artificially the ligaments were cut and the amount of shrinkage was measured

TABLE XVIII

	Distance between points		Difference mm	Per cent
	Before cut mm	After cut mm		
Lig anterior				
S 1 L5 disc level	20	18 5	1 5	7.5
L5 body vert level	30	28	[illegible]	6 6
Lig posterior				
S 1 L5 disc level	20	17.5	2.5	12.5
L5 body vert. level	30	27	3	10

TABLE XV

	Distance between points		Difference mm	Per cent
	Before cut mm	After cut mm		
Lig anterior				
L3 L2 disc level	23	16	7	30 4
L4-L3	20	15	5	25
L3 body vert level	25	20	5	20
Lig posterior				
L3 L2 disc level	20	10	10	50
L4-L3	20	12	8	40
L3 body vert level	25	15	10	40

In order to determine the shrinkage of ligaments from a segment of the lumbar spine where intradiscal pressure was not raised artificially the ligaments were cut in similar fashion at the levels of the S 1—L5 disc and L5 body vertebra

Results

TABLE XVI

	Distance between points		Difference mm	Per cent
	Before cut mm	After cut mm		
Lig anterior				
S1 L5 disc level	25	23	2	8
L5 body vert level	25	23	2	8
Lig posterior				
S1 L5 disc level	10	8 5	1 5	15
L5 body vert level	25	22	3	12

The shrinkage of the ligaments from segments of this vertebral column where the intradiscal pressure was not artificially raised did not differ from the shrinkage observed in the samples of ligaments studied from segments of other vertebral columns in previous experiments

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Results

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	Distance between points		Difference mm	Per cent
	Before cut mm	After cut mm		
Lig ant or				
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L4 L3	20	19 5	0 5	2.5
L3 body	20	19.5	0 5	2 5
Lig po t r				
L3-L2 d sc level	20	18 5	1 5	7 5
L4-L3	20	19	1	5

On the level of S 1—L5 where the intradiscal pressure was not decreased artificially the ligaments were cut and th amount of shrinkage was measured

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	Distance between points		Difference mm	Per cent
	Before cut mm	After cut mm		
Lig anterior				
S 1 L5 disc level	20	18.5	1.5	7 5
L5 body vert level	30	28	2	6 6
Lig posterior				
S 1 L5 disc level	20	17.5	2.5	12.5
L5 body vert. level	30	2[illegible]	3	10

TABLE XV

	Distance between points		Difference mm	Per cent
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L3 body vert level	25	15	10	40

In order to determine the shrinkage of ligaments from a segment of the lumbar spine where *intradiscal pressure was not raised artificially the ligaments* were cut in similar fashion at the levels of the S 1—L5 disc and L5 body vertebra

Results

TABLE XVI

	Distance between points		Difference mm	Per cent
	Before cut mm	After cut mm		
Lig anterior				
S1 L5 disc level	25	23	2	8
L5 body vert level	25	23	2	8
Lig posterior				
S1 L5 disc level	10	8 5	1 5	15
L5 body vert level	25	22	3	12

The shrinkage of the ligaments from segments of this vertebral column where the intradiscal pressure was not artificially raised did not differ from the shrinkage observed in the samples of ligaments studied from segments of other vertebral columns in previous experiments

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Increase in the intradiscal pressure causes an increase in the prestress of the longitudinal ligaments of the vertebral column

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Using a thick needle and instruments used *routinely for the extirpation* of the nucleus pulposus the nuclei of the discs L4—L3 and L3—L2 were removed At a distance of 3 cm two points were marked on both the anterior and posterior longitudinal ligaments at the level of the L3 vertebral body In addition two points were marked at 2 cm separation on both ligaments between the levels of L4—L3 and L3—L2 The ligaments were then cut and the distance between the points was again measured

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	Distance between points		Difference mm	Per cent
	Before cut mm	After cut mm		
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L4-L3	20	19 5	0 5	2 5
L3 body	20	19.5	0 5	2 5
Lig posterior				
L3-L4 disc level	20	18 5	1 5	7 5
L4-L3	20	19	1	5

On the level of S 1—L5 where the intradiscal pressure was not decreased artificially the ligaments were cut and the amount of shrinkage was measured

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	Distance between points		Difference mm	Per cent
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L3 L2 disc level	20	10	10	50
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L3 body vert level	25	15	10	40

In order to determine the shrinkage of ligaments from a segment of the lumbar spine where intradiscal pressure was not raised artificially the ligaments were cut in similar fashion at the levels of the S 1—L5 disc and L5 body vertebra

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	Distance between points		Difference mm	Per cent
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The shrinkage of the ligaments from segments of this vertebral column where the intradiscal pressure was not artificially raised did not differ from the shrinkage observed in the samples of ligaments studied from segments of other vertebral columns in previous experiments

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Increase in the intradiscal pressure causes an increase in the prestress of the longitudinal ligaments of the vertebral column

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	Distance between points		Difference mm	Per cent
	Before cut mm	After cut mm		
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L3 L2 d sc le el	20	19	1	5
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L3 body	20	19.5	0 5	_5
Lig poster o				
L3 L_ disc level	20	18.5	1 5	7.5
L4-L3	20	19	1	5

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In order to determine the shrinkage of ligaments from a segment of the lumbar spine where intradiscal pressure was not raised artificially the ligaments were cut in similar fashion at the levels of the S 1—L5 disc and L5 body vertebra

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CONCLUSION

Increase in the intradiscal pressure causes an increase in the prestress of the longitudinal ligaments of the vertebral column

TABLE XIX

Samples of equal dimensions (1 mm)

	Average shortening of lig		Corresponding load gm	
	Anterior	Posterior	Anterior	Posterior
Non-degenerated	10 9	13 4	20—25	50—65
Degenerated	7 1	9 0	10—20	45—50

As the above values of preload were determined for small samples of the ligaments approximate calculations of total ligament preload were performed These calculations based on the average dimensions of the ligaments gave us values for group 1 of 200—250 gm for the anterior longitudinal ligament and 225—350 gm for the posterior longitudinal ligament. Similarly in group 2 150—200 gm for the anterior and 225—250 gm for the posterior longitudinal ligament were the values obtained

In order to check the above calculations 12 samples of full ligament cross section were loaded to 5 Kg From two lumbar spines (nos 42 44 Table I) 6 samples were obtained from the anterior and 6 from the posterior longitudinal ligaments (This represented three samples from each of the ligaments of each of the spines) In one lumbar spine there were no degenerative changes present whereas in the other both macroscopic and microscopic changes were of the order of grades 3 or 4 From the curves obtained during the loading of these samples it was then possible to calculate the average value of force corresponding to 10 9 13 4 7 1 and 9 0 per cent strain respectively and these values were as follows

TABLE XX

Samples of full cross section

	Average shortening of l g		Corresponding load gm	
	Anterior	Posterior	Anterior	Posterior
Non-degenerated	10 9	13 4	180	300
Degenerated	7 1	9 0	120	180

CONCLUSION

The exact determination of the preload value for the longitudinal ligaments is very complicated Results may differ markedly since the dimensions of the ligaments vary It is however possible to demonstrate that prestress exists and has a value between 120—350 gm It appears that the prestress is dependent on the pressure within the nucleus pulposus and on the elasticity of the annulus fibrosus

CONCLUSION

Decrease in the intradiscal pressure causes a decrease in the preload in the longitudinal ligaments

General conclusions

The above experiments lead to the conclusion that the longitudinal ligaments exist in a prestressed state due to the condition of the intervertebral discs On removal *from the vertebral column the ligaments shrink* as they are no longer subjected to this tensile force The amount of shrinkage or shortening following removal depends on the amount of prestress and this varies with the state of both the intervertebral disc and the annulus fibrosus In young people in whom the intervertebral disc as well as the annulus fibrosus is intact, the prestress is greater and *thus the subsequent shrinkage or shortening is greater As degenerative* changes occur with the concomitant destruction of the intervertebral disc the prestress becomes lower which follows the known reduction in nuclear pressure

Approximate prestress of the anterior and posterior longitudinal ligaments

Experiments carried out on the shortening of ligaments following their removal from the spine showed that the anterior and posterior longitudinal ligaments did not shorten equally The anterior *longitudinal ligaments shortened less than the* posterior In addition we noted that degenerative changes of the intervertebral disc had a definite bearing on the subsequent shortening of the ligaments Ligaments obtained from spines without degenerative changes or those of grade 2 degeneration shortened significantly more than those obtained from spines where *the intervertebral discs were destroyed*

It was observed that in the group of healthy or slightly degenerated spines the anterior longitudinal ligament *shortened following* preparation by *10 9 per cent* and the posterior by 13 4 per cent Similarly in the second group that is those with degenerative changes of grade 3 or 4 the anterior longitudinal ligaments shortened by 7 1 per cent and the posterior by 9 0 per cent

On the curves obtained from loading experiments the loads which corresponded *respectively to 10 9 13 4 7 1* and *9 0 per cent stretching of the samples* were determined (see Table XIX)

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Samples of equal dimensions (1 mm)

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TABLE XIX

Samples of equal dimensions (1 mm²)

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	Anterior	Posterior	Anterior	Posterior
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TABLE XX

Samples of full cross section

	Average shortening of lig		Corresponding load gm	
	Anterior	Posterior	Anterior	Posterior
Non-degen rated	10 9	13 4	180	300
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CONCLUSION

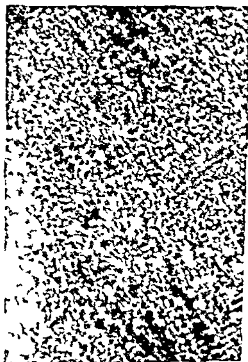
The exact determination of the preload value for the longitudinal ligaments is very complicated Results may differ markedly since the dimensions of the ligaments vary It is however possible to demonstrate that prestress exists and has a value between 1 0—350 gm It appears that the prestress is dependent on the pressure within the nucleus pulposus and on the elasticity of the annulus fibrosus

VIII MICROSCOPIC INVESTIGATION OF THE LONGITUDINAL LIGAMENTS SUBJECTED TO LOADING

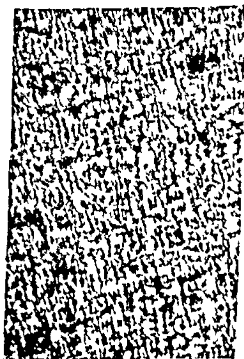
In order to determine what happens to the collagenous fibres of the ligaments during loading the following investigations was made Samples of 0 05 mm thickness were obtained from both the anterior and posterior longitudinal ligaments (specimen nos 12 51, 61, Table I) They were placed under a microscope and the following observations were recorded photographically using 100 fold magnification The samples were subsequently stretched using small hooks arranged in such a way that the loading could be increased by the addition of weights With each load increment a photograph of the specimen was taken

It was noted that the collagenous fibres of fully relaxed ligaments were not visible However rows of light and dark spots were observed and these appeared to be arranged into regular stripes (Fig 9 a b c d) On initial loading the outlines of the fibres appeared and the light and dark spots began to vanish With increased loading the outline of the collagenous fibres became more distinct and

Fig 9 Micrographs of the l gament subjected to uniaxial load (x 100)



a/unloaded



b/approx 15% failure stress



c/approx 30°° failure stress



d/approx 60 ° failure stress

the light and dark spots vanished completely As the loading is further increased one could see a distinct reorientation of the fibres into the line of the force The fibres then began to glide upon one another until the sample tore

CONCLUSION

It is possible to study under an ordinary microscope collagenous fibres without using stains which change the tensile properties of these fibres Employing a system which allows for increments in loading one can observe the behaviour of collagenous fibres subjected to increasing load During loading the collagenous fibres rearrange themselves parallel to the axis of stress The greater the tensile stress the more complete the rearrangement of the fibres As the failure load is approached there is a relative gliding of fibres and this represents the breaking of the forces which hold the fibres together It is only when these forces are broken that the fibres tear completely

IX STUDY OF THE TENSILE PROPERTIES OF THE LIGAMENTS AS RELATED TO DEGENERATIVE CHANGES, AGE AND LEVEL

The degeneration of the lumbar spine is a common process occurring in adult life The earliest changes possible to find occur in the discs Hirsch (1951 1954) Nachemson (1960), Rolander (1966) and Galante (1967) have demonstrated that changes in the physical properties of the disc are a function of the degenerative process In order to investigate the influence of degenerative processes and age on the tensile properties of the anterior and posterior longitudinal ligaments the following studies were performed on samples from cadavers 1 day to 67 years of age (Table I nos 34—64)

Effect of degeneration, age and level

206 samples from 30 lumbar spines were investigated

In order to describe the degree of degeneration the material was graded macroscopically according to the criteria described under 'Materials and Methods (see page 27) Subsequently the roentgenograms were analyzed and a histological study was made of both the annulus fibrosus and the ligaments The material was then divided into three groups using the following criteria

Group 1 Those without degenerative changes

Group 2 Those with degenerative changes qualifying for group 2 according to macroscopic criteria (see page 19) and without radiographic changes Histologically degenerative changes such as cavities filled with granulation material and partial cartilagenous metaplasia

Group 3 Marked degenerative changes visible macroscopically qualifying for group 3 and 4 (see page 19) Radiologically osteophytes as well as narrowing of intervertebral discs Histologically fissures in the annulus which are filled with vascularized fibrous tissue and pronounced cartilage metaplasia (Hirsch and Schajowicz 1952)

To analyze the tensile properties in samples from non degenerated and degenerated specimens the following computations have been made 143 non degenerated samples and 63 degenerated samples have been subjected to multiple regression analysis

This analysis yields an equation of the form

$$Y = C_0 + C_1 A + C_2 A^2 + C_3 L$$

with regression coefficients C_1 C_2 C_3 showing the influence of age (A) and level (L)

To detect discrepances resulting from the linear influence of age a term consisting of the square of A has been put into the model

The dependent variable Y has been subsequently calculated from values of deformation residual deformation and energy dissipation

The results are as follows

TABLE XXI

Deformation mm

Non degenerated $Y = 0\ 64 - \underline{0\ 0072\ A} + \underline{0\ 00007\ A^2} + \underline{0\ 0259\ L}$

Degenerated $Y = 8\ 68 - \underline{0\ 26\ A} + \underline{0\ 0002\ A^2} + 0\ 01\ L$

Residual deformation mm

Non degenerated $Y = 0\ 17 - \underline{0\ 0018\ A} + 0\ 00001\ A + \underline{0\ 0066\ L}$

Degenerated $Y = 1\ 82 - 0\ 05\ A + 0\ 0004\ A^2 + \underline{0\ 005\ L}$

Energy dissipation gm mm

Non degenerated $Y = 4\ 12 - \underline{0\ 04\ A} + 0\ 0002\ A^2 + \underline{0\ 17\ L}$

Degenerated $Y - 35\ 76 - 1\ 04\ A + 0\ 008\ A^2 + \underline{0\ 15\ L}$

CONCLUSION

The underlined regression coefficients are significantly different from zero at the 5 per cent level In the non degenerated material the coefficients for age and level are always significant and the coefficient for A² is just significant for deformation

An analysis of variance for the whole regression model that *is comparing the* sum of squares due to regression with the sum of squared deviations from the estimated regression equation showed that the variance is significant for every measurement in the non degenerated material but not in the degenerated material This is due to the spread in the measurements and the fact that a very *restricted interval of age was considered*

Effect of degeneration

TABLE XXII

Means and standard errors of the results from degenerated and non degenerated samples in the age range 45—70 years

	Degenerated	Non degenerated
Deformation mm		
Mean	0 46	0 53
S E	0 068	0 076
Residual deformation mm		
Mean	0 12	0 15
S E	0 026	0 024
Energy dissipation gm mm		
Mean	3 11	3 33
S E	0 68	0 61

These are the means and standard errors calculated with no attention paid to differences between anterior and posterior ligaments age or level They make one suspect that there are differences between degenerated and non degenerated samples To analyze such a difference six samples from degenerated specimens were selected These were paired with six samples from the non degenerated material The purposes of pairing are as follows

The samples were from specimens of the same age and the same level and the anterior and posterior ligaments corresponded

For each parameter the differences between the non degenerated samples and the degenerated samples were calculated

To test whether the mean difference could be considered as zero a t test was performed

The results of these test procedures are as follows

TABLE XXIII

	Deformation mm	Residual deformation mm	Energy dissipation gm mm
Mean difference	0 14	0 03	0 6
Standard error of difference	0 07	0 01	0 95
Computed t value	5 12	8 85	1 47

CONCLUSION

Deformation and residual deformation were significantly larger in the non degenerated group of samples No significant differences were observed in the energy dissipation

Effect of age

In order to study the influence of age from degenerated samples the mean level has been put into the equations giving the following

TABLE XXIV

Deformation mm	$Y=0.73-0.0072\,A+0.00007\,A^2$
Residual deformation mm	$Y=0.19-0.0018\,A+0.00001\,A^2$
Energy dissipation gm mm	$Y=4.67-0.0361\,A+0.00020\,A^2$

The regression coefficients are still the same
The equations are illustrated graphically (Fig 10 11 12)

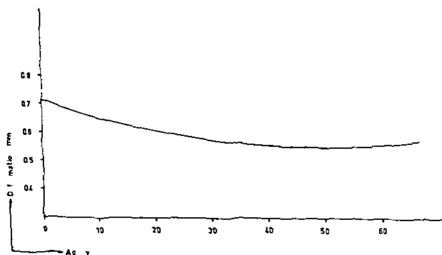


Fig 10 Mean level of total deformation as a function of age Non-degenerated samples

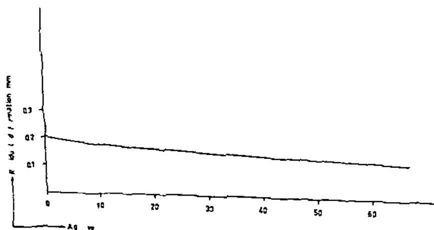


Fig 11 Mean level of residual deformation as a function of age Non-degenerated samples.

	Degenerated	Non degenerated
Deformation mm		
Mean	0 46	0 53
S E	0 068	0 076
Residual deformation mm		
Mean	0 12	0 13
S E	0 026	0 024
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In order to study the influence of age from degenerated samples the mean level has been put into the equations giving the following

X DISCUSSION

The anterior and posterior longitudinal ligaments lie on the anterior and posterior surfaces of the intervertebral discs and are attached to both the discs and the bodies In view of this relation it is evident that these ligaments will deform with any structural deformation of the disc which can be the result of forces acting on the disc or of structural changes These ligaments are richly innervated and thus their stimulation may give rise to the sensation of pain (Roofe 1940 Inman and Saunders 1944 Hirsch 1949 Wiberg 1949 Stilwell 1956 Pedersen Blunck and Gardner 1956 Hirsch Ingelmark and Miller 1963 Hollinshead 1965 Jackson Winkelman and Bickel 1966)

The longitudinal ligaments are in a state of prestress as is evidenced by their shrinkage following removal from the spine This state of prestress is maintained by the conditions of the discs

A histological study of unstressed ligaments has revealed a wave like configuration of the fibrous components which makes it difficult to distinguish separate fibres On loading the fibres become progressively polarized and eventually slide upon one another thus causing rupture of the tissue

During mechanical testing of the ligaments it was observed that the material stabilized in approximately 3 minutes of loading after which time it behaved elastically This time dependent phenomenon may depend on the fibres and their arrangement and on the properties of the ground substance

The *interrelationship* between the disc and the ligaments must be considered both statically and dynamically If we use certain simplifications in a *statical* analysis we can consider the relation between the disc and ligaments in two *distinct* cases i e when the disc faces of the vertebral bodies are parallel or angulated In order to determine the *change in a force* acting on a segment of the ligament adjacent to a disc and how this *force is* dependent on the angle that the adjacent vertebrae form with each other the following system was analyzed (see Fig 13)

The cartilaginous end plate of L5 was designated A and the cartilaginous end plate of S 1 was designated B The anterior and posterior segments of the ligaments within the limits of the disc were designated a and b respectively and the theoretical analysis was carried out by making the following assumptions

1) That this is a system consisting of the fibres of the ligaments connected to those of the annulus fibrosus which in turn enclose the semi fluid gelatinous substance of the nucleus pulposus

2) That the disc is normal A force analysis was carried out on the segment between L5 and S 1 but such a technique may be employed at all other levels provided the variable angle alfa, is altered accordingly (see diagram)

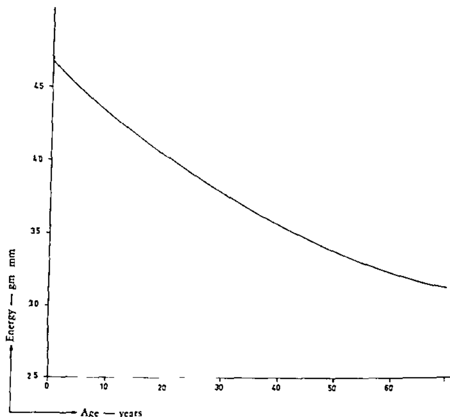


Fig 12 Mean level of energy dissipation as a function of age Non-degenerated samples

CONCLUSION

In the young elongation and residual deformation decreased progressively with age After 20—30 years of age changes occur more slowly The rate of change in energy dissipation decreases after the age of 40 years

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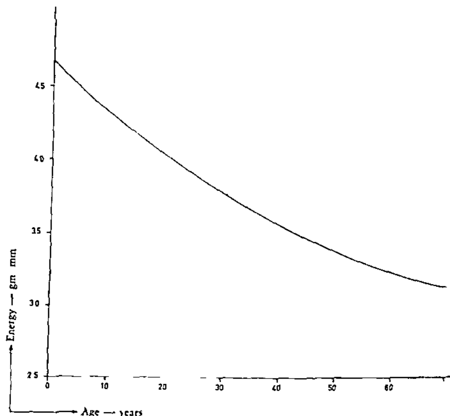


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Fig 13

Description of theoretical model

We shall assume that the disc is a distorted sphere with a radius R and is loaded from above by the element A which is the surface of the vertebral body exerting a force G at right angles to the surface A The deformed sphere (disc) rests on the surface B which is the surface of the vertebral body below where surface area is not parallel to A but makes an acute angle alfa with A Any force which acts at right angles to the tangent drawn at a point either on the outer or inner surface of the sphere (nucleus pulposus) is transmitted through the outer layer of this sphere The pressure within the system we shall designate P and the thickness of the wall of the sphere (annulus fibrosus) g We shall assume that the angle alfa does not exceed 15°

In the analysis of this system the force G acting on this sphere and on the element B its support may be resolved into its components N which is perpendicular to the surface B and the tangential component S These two component forces S and N acting on A produce a shear and compression with respect to B Disregarding the accuracy of force transmission by the shear on B one can conclude that the stresses in the walls of the container where they come

in contact with the elements A and B will be dependent on the Force S The magnitude of this force S is G sin α The force N exerts a pressure on B equal to G cos α The force N diminishes as the angle α becomes greater If the two elements A and B are parallel to each other then the angle α is zero and the pressure P is dependent upon the force G and is given by $P = \frac{G}{F}$ where F is the contact area of the element with the sphere

The stress within the wall is assumed to be $\sigma = \frac{P \; R}{2g}$ where R is the radius of the wall and g the thickness of the wall As changes take place in the angle α there is effective a variable angle β of the wall considered to be approximately 1 3 of the circumference (see diagram) There is a further stress which is brought about by the force S in this segment as $\sigma_s \cong \frac{S}{g \; \frac{2}{3}\pi R}$ which is in addition to the stresses brought about by the pressure P Although the stress σr and σd do not add directly because they act in different directions their combined effect may be expected to be more severe than either one acting alone In order to obtain numerical values we must then get an average value in every case for the radius R the thickness of the wall g (annulus fibrosus) as well as the area of contact of the sphere with the vertebral body F

When the angle α is zero or has a very small value the annulus fibrosus can tolerate a high loading and the ligaments in contact with the annulus are exposed to small tensile stresses In the lower segments where the angle alfa is relatively large the tolerance of the annulus is much lower and one can reach the

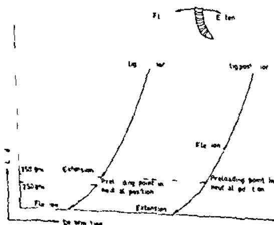


Fig 14

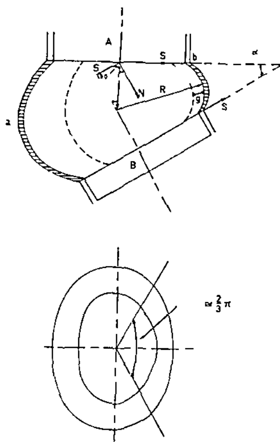


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In the analysis of this system the force G acting on this sphere and on the element B its support may be resolved into its components N which is perpendicular to the surface B and the tangential component S These two component forces S and N acting on A produce a shear and compression with respect to B Disregarding the accuracy of force transmission by the shear on B one can conclude that the stresses in the walls of the container where they come

XI SUMMARY

The aim of this programme was to investigate in vitro the tensile characteristics of the *longitudinal ligaments of the human lumbar spine* and to determine the influence on these properties of age and degeneration The material for this work was obtained from 74 lumbar spines taken from cadavers in the age range 1 day to 92 years In all 484 samples of the longitudinal ligaments were tested

Preliminary experiments were performed in order to evaluate and develop the proposed experimental techniques

While preparing ligament samples of standard dimension it was observed that a significant water loss occurred during 3 minutes of exposure to ambient air (60—70 per cent relative humidity and 20—28°C) In an attempt to prevent this dehydration a number of ligament samples were immersed in distilled water Ringer solution human plasma or Macrodex Within 3 minutes all samples were found to have absorbed a significant amount of fluid the greatest uptake occurring in distilled water and the least in human blood plasma.

A similar experiment was performed on samples exposed for one hour to water saturated air and no significant change in weight was observed

In the above experiments there was no significant difference between the behaviour of the anterior and posterior ligaments

Subsequent experiments were performed in a high humidity chamber containing air at 100 per cent relative humidity and 25—28°C and a similar environment was employed during sample preparation

In order to obtain samples of ligaments of uniform thickness sheets from the ligaments were cut on a Cryo-microtome the ligaments having been frozen to a temperature of —60°C Investigations showed that rapid freezing and subsequent thawing had no significant effect on the tensile properties Once the experimental techniques had been established *the test programme* proper was initiated

The first experiment was to determine the *failure load* of the ligaments and it was observed that the anterior ligament is stronger than the posterior These results are scattered as the dimensions of ligaments from each lumbar spine showed a considerable variation In order to obtain comparable results standard samples of the ligaments (of dimension 0 5×2 mm and 9 mm distance between the test clamps) were introduced Such samples were found to have average failure loads of 2 12 kg and 1 98 kg for the anterior and posterior ligaments respectively and this was independent of the level of the lumbar spine from which the samples were obtained In samples from severely degenerated spines failure occurred at substantially lower loads In the investigation of all the other parameters a maximum load of 0 5 kg was employed as this approximates to 30 per cent of the average failure load

point of rupture much sooner In this case the ligament is subjected to much higher forces and strains Once degenerative changes take place the annulus thins and undergoes much greater deformation which causes excessive stretching of the posterior longitudinal ligament At the moment when the annulus ruptures the above described analysis ceases to hold

During flexion and extension of the lumbar spine the longitudinal ligaments adjust to the position of the vertebral column and thus either lengthen or shorten It is probable that the ligaments only work during a certain phase of loading which may be illustrated by the following load/deformation curve (see Fig 14)

As the disc space decreases the ligaments have to function in the toe part of the curve When the ligaments are subjected to rapid deformation during movement of the spine then the peak forces induced could be larger than those developed in a wholly elastic material

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Subsequent cyclic loading experiments (35 second intervals) were conducted to determine the difference between the tensile properties of the anterior and posterior ligaments as well as the dependence of these properties on the level of the lumbar spine from which the samples were obtained

A statistical analysis of the results obtained from the experiments disclosed the following

There is a significant difference between the tensile properties of the anterior and posterior ligaments In the second and third load cycles the difference between the deformation of these ligaments is not significant

The tensile properties of both ligaments are dependent on the level of the lumbar spine The shrinkage of ligaments occurring on separation from the lumbar spine suggested that these ligaments are in a state of prestress and experiments conducted with increased and diminished intradiscal pressure led to the conclusion that this prestress is dependent on the condition of the disc

Values of the prestressing were calculated from experiments performed on samples of standard dimensions and were substantiated by similar experiments on whole ligaments In non degenerated specimens the preload was 200—250 gm in the anterior ligament and 225—350 gm in the posterior However in degenerated specimens the values of preload were 120—200 gm and 225—250 gm for the anterior and posterior ligaments respectively

Histological investigation on unstained ligament sections showed that there is a progressive polarization of the collagen fibre bundles with increasing stress No orderly fibre structure was evident in unstressed samples but with the progressive application of load an increasing proportion of the fibres was reorientated parallel to the axis of stress

The extensibility of both the anterior and posterior ligaments was found to decrease rapidly with ageing but after 20—30 years this progression of stiffening is less marked

Both deformation and residual deformation were significantly smaller in samples obtained from the degenerated spines than in the normal samples

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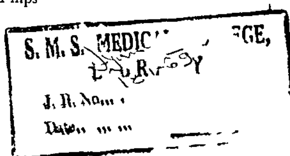
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P SALENIUS AND R KIVILAAKSO

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A survey of 99 treated hips



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ACTA ORTHOPAEDICA SCANDINAVICA
SUPPLEMENTUM No 114

From the Orthopedic Hospital of the Invalid Foundation Helsinki
(Head Professor Anders Langenskiold M D)

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P SALENIUS and R KIVILAAKSO

MUNKSGAARD
COPENHAGEN 1968

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INTRODUCTION

Slipping of the upper femoral epiphysis has at all times offered a difficult orthopedic problem with regard to etiology early diagnosis and choice of treatment The problem is particularly important because it affects young patients for whom the result of treatment is vital for their later years

From time to time other names have been used for this disease such as epiphyseal fracture adolescent rickets bending of the femoral neck, adolescent or epiphyseal coxa vara arthritis deformans juvenilis and femoral osteochondritis of adolescents

Pare in 1572 is thought to have been the first to describe slipping of the upper femoral epiphysis (Howorth 1966)

It was not until last century however that positive development in diagnosis began and a growing number of descriptions of cases appeared in the literature In 1868 Colignon collected all cases presented till then a total of 10

Bousseau in 1867 at an autopsy was the first to note slipped upper femoral epiphysis in a 15 year old boy fatally injured by a cart The autopsy showed a capital epiphysis completely detached from the femur Wright in 1887 made a further report from an autopsy affecting a 40 year old woman She had suffered a complete slipping of the capital epiphysis in childhood Muller in 1888 published 4 cases In one of these the femoral head had been removed because the lesion was considered tuberculous

At the end of the 19th century more and more reports appeared each dealing with 3–4 cases In 1898 Poland published an extensive monograph 'Traumatic separation of the epiphysis containing the cases which had appeared in the literature up to then 31 in all He added one case of his own All these published cases had been diagnosed without radiological confirmation on the basis of symptoms the pathological picture of operative or autopsy finding alone After roentgenography came into use in 1895 more cases were noted and the number of publications increased However the disease was still considered fairly uncommon since even at the beginning of the century

Harris (1950) published an experimental study of the upper epiphyseal plate of rats tibia He divided the rats into 3 groups each comprising ten animals Group 1 consisted of control animals In group 2 gonadectomy was performed and 1 mg growth hormone administered daily In the third group oestradiol was given 3 times weekly It was then observed that the strength needed for detachment of the upper tibial epiphysis of rats treated with growth hormone was only half of that required for detachment of the tibial epiphysis of control animals In oestradiol treated rats this strength was 50 per cent greater than in control animals and 3 times greater than in rats treated with growth hormone after gonadectomy For this reason the author concludes that slipped capital epiphysis in adolescents may have two main causes First that sex hormone secretion is abnormally low as in patients with overweight and underdeveloped genitals and second that growth hormone secretion is abnormally high and growth sudden as clearly appears in tall thin quickly growing children Obviously in such cases no great importance attaches to the hormone secretion value in itself but to the relation between growth and sex hormone Thus if sex hormone secretion is very low as in patients with overweight growth hormone secretion may be normal or sub normal but it is abnormally high in relation to sex hormone secretion and may cause weakening of the epiphyseal plate against tangential strain

Clinical experience experimental study and endocrinological observation all support the opinion that hormonal factors have a great perhaps decisive influence on the etiology of slipped upper femoral epiphysis A normal capital epiphysis may of course be detached as a result of powerful trauma but these cases are very rare

DIAGNOSTIC ASPECTS

Slipped upper femoral epiphysis usually causes pain in the hip and more rarely in the knee Patients are commonly children aged 9—15 An ordinary antero-posterior X ray shows slipping of the capital epiphysis as follows

1 Normally the capital epiphysis protrudes over the upper lateral edge of the neck in the antero-posterior x ray and appears as a prominence outside the femoral neck The slightest slipping causes this projection to disappear which is considered by some investigators to be the first symptom (Jerre 1950)

publications dealing with only 1—6 cases appeared In 1926 Key published 24 cases diagnosed at Massachusetts General Hospital In 1931 Fergusson and Howorth published 70 cases from New York Orthopedic Hospital over 20 years Howorth's cases by now number more than 200 (1966)

ETIOLOGY

Opinions on the etiology of slipped upper femoral epiphysis have varied considerably in the course of the centuries Duverney (1751) supposed that the condition arose from some other disease such as syphilis or tuberculosis In the 19th century there was much discussion on the etiology of the disease as the number of cases noted increased Muller (1888) believed that it was an after effect of rickets, as did Schultz (1892) Trauma was considered an important reason for the origin of slipped upper femoral epiphysis especially as cases previously published were usually a consequence of trauma

It has been generally recognised, especially during this century, that most cases occur in patients who are at the strongest stage of growth and are somewhat overweight or abnormally tall or both For this reason it is widely believed that the cause of the disease is an endocrine disturbance On the other hand, not all cases are bilateral The number of bilateral cases, however, varies considerably in different reports Howorth (1957), for instance states that 14 per cent of cases are bilateral, Jerre (1950) 41 8 per cent and Klein et al (1953) 41 per cent But Billing and Severin (1959) in an extensive monograph based on thorough radiological study have come to the conclusion that bilateral cases or their after effects account for as much as 80 per cent

Lofgren in 1953 examined 16 cases treated for slipping upper femoral epiphysis with an endocrinological background especially in mind He observed that in all these cases the sella turcica was abnormally small His material included 2 pituitary tumors Also the majority of the male patients had an endocrine defect in the form of overweight Burrows (1957) also examined the endocrinological background in an extensive study Urinary ketosteroid secretion was normal The conclusion was reached from other information and clinical evidence, that one quarter of the boys and almost two thirds of the girls suffered from endocrine disturbance in addition to those who were overweight

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2 When the epiphysis slips backward its thickness (measured from the epiphyseal line to the joint surface) decreases in proportion as the slipping increases

3 Waldenstrom *states (1939) that even at an early stage of slipped* upper femoral epiphysis the surfaces of the epiphysis and metaphysis become irregular and no longer fit together In the roentgenogram this is seen as an irregularity of the epiphyseal line

Although in the antero posterior picture slipped epiphysis can thus be diagnosed in some cases, the lateral view is quite indispensable whenever slipped capital epiphysis is suspected The lateral exposure can be taken in various positions (Billing and Severin 1959) Some maintain that a pre slipping stage exists in which the epiphyseal line has merely widened and its outlines are obscure (Fergusson and Howorth 1931, Jerre 1950, Howorth 1957 and 1960) The pre slipping stage it is stated, produces symptoms with pain in the hip (Fahey et al 1965) Waldenstrom (1939) believes that in such a stage no symptoms are produced and the slipped epiphysis can be detected only *from an X ray picture Billing and Severin (1959)* main tain that slipped epiphysis can be detected at a very early stage as an angle between epiphyseal line and collum which appears in special X ray exposures

The degree of slipping of the capital epiphysis in relation to the neck may be expressed in many different ways In the literature some confusion is caused by the fact that a variety of terms are used Billing and Severin (1959) express slipping as an angle between epiphyseal line and neck Some ex press slipping in inches (Howorth 1957), while others speak only of slight *or market slipping (Ferre 1950) More specific measurements* have also been published Some have divided cases into groups of minimal quarter, half three quarter and total slipping (Burrows 1957), others speak of slight, minim al 1/4—1/3 half 2/3 (Hall 1957) Newman (1960) classified the position of epiphysis as acceptable or unacceptable Displacement of the epiphysis has been measured in centimetres by Klein et al (1953) Durbin (1960) considers that when slipping is over half the breadth of the epiphysis i e 50 per cent, the prognosis is considerably worse than in milder cases Most investigators have given up measuring the angle between epiphysis and neck because of uncertain results The main reason for this uncertainty is that in the X ray the hip must be in exactly the same position on every occasion which is impossible because *of restricted movements in the hip (Jerre 1950)* For this reason the di placement is perhaps most exactly expressed as a measure of length or even better as a relative part of the extent of the epiphysis

TREATMENT

Conservative treatment

Opinions on the relative merits of conservative and operative treatment are somewhat conflicting Operative treatment which leads to a moderate or poor result may be criticised on the ground that necrosis of the head may not appear in untreated cases and in cases of deformity coxarthrosis does not occur until a later age (Howorth 1957) Conservative treatment may in turn be criticised on the grounds that it is usually prolonged and results are often worse than those produced by operative treatment (Green 1945 Howorth 1949 Jerre 1950)

Conservative treatment mainly involves rest in bed traction walking on crutches walking with the aid of a Thomas splint and plaster immobilisation and a combination of all these

Jerre in 1950 examined the results of conservative treatment in a follow up and noted that in 21 cases of slight slipping results were good in 76 2 per cent fair in 19 per cent and poor in 4 8 per cent In 20 cases of greater slipping (marked) 5 per cent of results were good 85 per cent fair and 10 per cent poor Forrester—Brown (1941) examined 22 cases of conservatively treated slipped epiphysis part of which were treated by traction part by closed reduction and part by walking caliper Follow up was carried out on 11 patients only one of whom was able to move freely Nine had abduction adduction and rotation deficiency and all had some degree of flexion deficiency Howorth (1949) published results on 7 patients who had been treated by traction and then by plaster In no case was improvement achieved in the position of the epiphysis and results were poor in 6 cases Durbin (1960) treated 19 cases conservatively and obtained excellent results in 37 per cent good in 37 per cent fair in 5 per cent and poor in 21 per cent Hall (1957) treated 33 hips conservatively by various methods he states that manipulation produced some change in the position of the epiphysis in 24 cases and no change in 9 cases The best correction of the position was obtained in cases were a sudden slip had occurred Capital necrosis occurred in three cases where the condition of the epiphysis had improved it also occurred in two cases where no change had been produced In Hall s opinion manipulation is justified when performed with in a few weeks after sudden slip

It thus appears that although conservative treatment may achieve partially good results it may also produce necrosis of the head especially if manipulation or prolonged powerful traction is used Moreover conservative treatment is lengthy and results on the whole do not seem noticeably better than those produced by most methods of operative treatment

Operative treatment

In operative treatment an important question is whether the position of the capital epiphysis can be accepted or not If the capital epiphysis has slipped considerably, it may be asked whether the condition can be improved If the position of the head is acceptable the purpose of operative treatment is to prevent further slipping and several methods of fixing the epiphysis are possible If the slipping is severe the condition may be accepted even *then, and a mere fixation* may be considered sufficient, or one may try to improve the position of the head in relation to the neck A further alternative is to improve the position of the head and *neck by performing an osteotomy* in the neck or in the subtrochanteric or intertrochanteric part of the femur and fixing the head in its position

Fixation methods

The upper femoral epiphysis may be fixed to the neck by Smith Petersen nail (Wilson 1938, Wiberg 1941 1959 Fahey et al 1965, Lindstrom 1958) Other methods are by one or more pegs or screws (Fahey et al 1965, Durbin *1960,* Newman *1960,* Hall *1957,* Hiertonn *1955)* Fixation may *also be* performed by bone pegs (Fergusson and Howorth 1931) or by opening the epiphyseal line *and drilling a hole and implanting both* cortical bone and cancellous bone (Herndon et al 1963) Good results have been obtained by all these methods The large nail has been criticised for its tendency to push the loose head forward thus causing necrosis or splitting (Wiberg 1959 Howorth 1957) If, on the other hand, the nail penetrates at some point the joint cartilage and is not noticed or removed, arthrosis may develop sooner than usual (Wiberg 1959 Waldenstrom 1930) For this reason many *have advocated the use of thin pins (Moore pins) or screws for* fixation (Dunn 1964, Hall 1957)

In Wiberg s material of 185 cases the nail penetrated the joint cartilage in 15 cases final results were good however, because the position of the nail was corrected in some of the cases Capital necrosis appeared in two cases one of which was only partial

In Lindstrom s series (1959) of 51 nailed hips no case of capital necrosis occurred *Four cases were treated by manipulation* followed by nailing and in one of these capital necrosis occurred In Lindstrom's opinion the Smith Petersen nail is suitable and causes no complications when the slipping is slight

In Hall's material (1957) of 48 cases treated by Smith Petersen nail 5 cases of capital necrosis occurred but the author attributes them to other causes than the nail Excellent results were 68 9 per cent with the Smith Petersen nail 80 per cent with Moore pins Good results were 18 8 per cent with the Smith Petersen nail 20 per cent with Moore pins The latter produced no fair or poor results but the Smith Petersen nail produced 8 4 per cent poor

Newman (1960) performed fixation in 13 cases with the Smith Petersen nail One result was poor but the case had been treated for 3 months by traction In 2 cases subtrochanteric fracture occurred near the nail In 26 cases stabilisation was performed with Moore pins in one case the pin came out and re slipping occurred followed by recovery and consolidation in a bad position

Durbin (1960) achieved the following results by nailing excellent 57 per cent good 22 per cent fair 14 per cent poor 7 per cent from a total of 14 hips 27 hips in his series were fixed with Moore type pins and results were excellent 52 per cent good 37 per cent fair 11 per cent and poor nil

In Jerre's material consisting of 183 hips capital necrosis occurred in 20 cases only one of which was a result of nailing however Fifteen were the consequence of reduction and plaster immobilisation and 2 followed closed reduction and nailing One hundred and two cases were treated with plaster immobilisation

In Howorth's material of over 200 cases operated by his own methode the epiphyseal line failed to close in 4 cases but capital necrosis did not occur in a single instance

On the basis of the literature alone it appears that Howorth's method as reported by himself produces the best results

Open reduction and wedge osteotomy

Opinions differ as to when the extent of *slipping is such* as to necessitate correction of the position of the head Some maintain that one third of the extent or more causes deformity of the joint later (Hiertonn 1956 Wilson 1938) Others maintain half *the extent* or more (Durbin 1960) and others 1 cm or more (Klein et al 1953)

When the epiphysis is considered to have slipped too much by one of the above criteria the method of treatment depends on whether so-called acute slipping or chronic slipping is involved *In the former* case closed reduction may be attempted as it is considered that the epiphysis is movable in

Operative treatment

In operative treatment an important question is whether the position of the capital epiphysis can be accepted or not If the capital epiphysis has slipped considerably, it may be asked whether the condition can be improved If the position of the head is acceptable the purpose of operative treatment is to prevent further slipping and several methods of fixing the epiphysis are possible If the slipping is severe the condition may be accepted even then, and a mere fixation may be considered sufficient, or one may try to improve the position of the head in relation to the neck A further alternative is to improve the position of the head and neck by performing an osteotomy in the neck or in the subtrochanteric or intertrochanteric part of the femur and fixing the head in its position

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Linstrom in 1958 reported 24 wedge osteotomies with 2 caput necrosis 1 traumatic arthritis and 4 coxarthrosis

Other osteotomies

Subtrochanteric osteotomy and intertrochanteric osteotomy are indicated mainly in the late stage of slipped capital epiphysis in order to correct varus and external rotational deformity (Howorth 1966)

ASSESSMENT OF RESULTS

In the assessment of results confusion and difficulty have been caused by the fact that follow up intervals have differed in length methods of treatment have varied greatly and different methods have often been used in the same case Also the division of cases into excellent good fair' poor has sometimes been subject to variation

The patient s own assessment is used as first criterion Pain whether at rest or under strain is important Second to be used are results of objective follow up examination most important is the mobility of the hip As a rule mobility is assessed in various directions with points awarded for the degree of mobility attained Methods of calculation available are given by Gade (1947) and Fergusson and Howorth (1931) According to Gade values for a normal hip vary 85—100 points According to Fergusson and Howorth the index for a normal hip should be 85—95 (Fergusson and Howorth 1931 Howorth 1966) In clinical examination attention is also paid to limping discrepancy of length in limbs and the patient s ability to perform various activities (Hall Howorth Newman)

In X ray examination attention is given to the form of the femoral head and the joint surfaces also to possible secondary osteoarthritis or necrosis of the head or its cartilage

very recent slips Results are often unsatisfactory, however, and cases of capital necrosis have occurred (Jerre 1950, Howorth 1966)

For this reason it is the general opinion that closed reduction should not be performed except in very acute cases Results are uncertain even then

Open reduction

In late cases with an unacceptable degree of slip an open reduction or a wedge osteotomy can be performed

Open reduction has been performed since the latter half of last century but has been abandoned in many clinics because of capital necrosis Wilson in 1924 published 7 cases of open reduction 4 of which were fresh and 3 late slipping Fergusson and Howorth in 1931 published 11 cases of open reduction, and Badgley et al in 1948 11 cases, 6 of which produced good results Klein et al in 1948 reported 16 cases and Friberg (1948) 12 cases with one caput necrosis In 1966 Howorth reported 16 cases in which plaster was used after open reduction 5 were good 6 fair and 5 poor Seven were nailed after open reduction and of these 5 were good, 1 fair and 1 poor In the former group there was 1 case of caput necrosis and 7 cases of cartilage necrosis In the latter there were 6 cases of cartilage necrosis and none of caput necrosis Dunn (1964) reported 23 open reductions in which a wedge osteotomy of the neck was performed in the same operation Nineteen of these led to a good result In one case caput necrosis appeared, and in one case partial necrosis after nailing Cartilage necrosis appeared in two cases Open reduction is nowadays considered by some to be unsatisfactory be cause of the operative risk and technical difficulties (Howorth 1966)

Wedge osteotomy

Howorth in 1966 made a thorough assessment of the literature in which some 400 wedge osteotomies are reported by various authors and caput necrosis recorded in 30 per cent He added his own material of 9 cases after osteotomy 4 of these were immobilised in plaster and 5 with Smith Peter sen nail Results at follow up were good in 5 cases fair in 3 poor in one case Caput necrosis occurred in 2 cases and carrtilage necrosis in one

Wiberg in 1955 reported 12 cases only one of which gave rise to caput nec rosis the remainder being good In his opinion, however the operation should be limited to rare cases Hiertonn also in 1955 reported 38 hips oper ated in the same way there were 5 cases of caput necrosis and 9 of partial caput necrosis Results were good in 24 cases

Table 2

Reason for seeking treatment

Symptoms	Number of patients	Boys	Girls
Pain in hip	35	24	11
Limping	8	4	4
Pain in hip + limping	33	24	9
Pain in knee only	4	3	1
All	80	55	25

32 patients reported injury either immediately before seeking treatment or earlier but in most cases this was a mild one such as slipping on the stairs falling from a bicycle or falling when walking *Only 6 patients* sought treat ment immediately in the other cases the symptoms were of several months *duration* Four patients complained of pain in the knee In 17 cases the patient had been treated elsewhere either on an incorrect diagnosis or no diagnosis *had been reached In* several cases no X ray had been taken or only an antero-posterior one In some of these cases no distinct diagnosis had been *made A radiograph* taken in a Lauenstein position clearly showed slipped epiphysis in all these 17 cases

Degree of slipping

In the present material the degree of slipping was estimated as a displace ment of the capital epiphysis according to its extent in relation to the femoral neck

Slipping was estimated always from a lateral X ray taken in the so-called *Lauenstein position* Especially in bilateral cases it was *possible to follow* the changes in the epiphyseal line of the unaffected hip when the patient came for re examination *of the other hip which had been* operated on or treated earlier (Figs 1 and 2) Slipped epiphysis was then diagnosed at a very early stage when displacement *was either non-existent* or extremely slight (Figs 1 2 4 This type of slipped epiphysis was marked as slight Otherwise slipped epiphysis *was classified from the lateral exposure as under 1/3* (Fig 7) under 1 2 (Fig 5 and 6) over half (Figs 8—10 12 and 13) and complete (Fig 11 *When secondary* callus had formed in the lower posterior part of the neck between it and the head the degree of slipping was estimated *as it had* evidently been before callus formation

PRESENT MATERIAL

The material comprises all cases of slipped upper femoral epiphysis treated at the Orthopedic Hospital of the Invalid Foundation, Helsinki in the period 1947—1965 This makes a total of 80 patients, 55 boys and 25 girls

Table 1 shows the distribution of the patients according to the side affected

Table 1

Side affected

Affected Side	Number of *patients*	Boys	Girls
Left	41	27	14
Right	20	16	4
Bilat	19	12	7
All	80	55	25

The material contained *21* boys and *8* girls who were clearly overweight For part of these cases an endocrine defect was clinically evident One of the boys was also suffering from pituitary tumor and had received radio therapy The height of this boy at the time of follow up was 218 cm or 7 ft 3 ins One girl also had a brain tumor combined with hypopituitarism and one boy a clearly diagnosed endocrine disturbance

Patients sought treatment for various reasons Table 2 analyses the symptoms concerned

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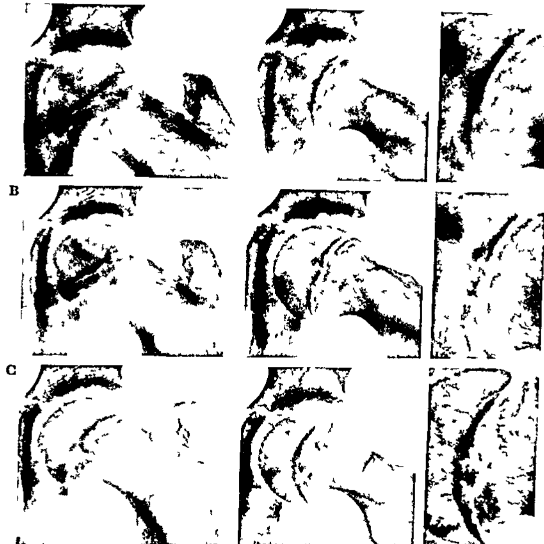


Fig 1 Left hip of a boy aged 14 at the time of nailing of the right hip 29 3 60
A — In the left hip the epiphyseal plate is regular The patient had no symptoms in this hip Lateral view on the right Enlarged view on its right side
B — Left hip 3 months after X ray in A In the middle of the epiphyseal plate in the lateral view the start of loosening in the form of irregularity No displacement as yet The antero posterior view does not show any sign of beginning of slip The patient did not feel pains in the hip The enlarged view of the epiphyseal plate on the far right
C — The patient felt slight pain in the left hip The antero posterior view is still normal Roentgenogram taken 5 months after A and 3 months after B The epiphyseal plate is irregular especially in the middle of the lateral view Slight slip The epiphysis was fixed by nailing (Fig 4) In this case the patient felt slight pain at the time of the beginning of slipping but in the lateral view signs of this could already be seen before that

Symptoms and earlier treatment

Table 3 shows duration of symptoms at various degrees of slipping

Among the bilateral cases were 11 in which slipped epiphysis was detected at an early stage when the patient came for re examination of a hip that

Table 3

Duration of symptoms

Degree of slipping	Number of hips	Under 1 month	Symptoms 1–2 m	2–6 m	6–12 m	Over 1 year
Slight	18	9	0	4	4	1
Under 1/3	26	0	1	11	10	4
Under 1/2	24	4	1	8	5	6
Over 1/2	29	1	0	14	7	7
Complete	2	0	0	1	1	0
All	99	14	2	38	27	18

had been treated earlier Six of these had pains five did not Ten cases in which the symptoms had lasted less than 6 months had been in traction earlier In ten cases with symptoms lasting less than 6 months the slipping had not been diagnosed and one had been given operative treatment elsewhere The remainder had received no previous treatment In one case where the symptoms had lasted over a year the patient had been treated for tuberculosis of the hip elsewhere In 5 cases where the symptoms had lasted over 6 months traction treatment had been given in 5 cases slipped epiphysis had not been diagnosed in 2 cases operative treatment had been given One of these was a case in which open reduction had been attempted elsewhere The attempt failed and was followed by complete slipping

The time interval between the slipping in the first affected hip and the slipping in the other hip in bilateral cases is shown in Table 4

Table 4

Time interval between first and second hip in bilateral cases

Interval between slipping	No Hips	Boys	Girls
Under 1 m	6	4	2
1–2 m.	3	1	2
2–6 m	2	2	0
6 12 m	3	3	0
Over 12 m	5	2	3
All	19	12	7

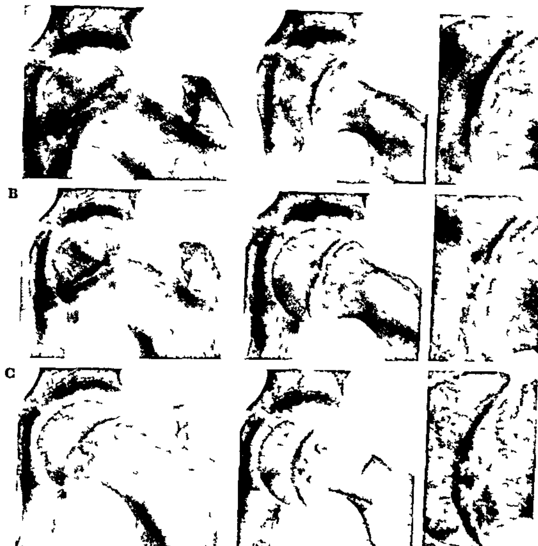


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1–2 m	3	1	2
2–6 m	2	2	0
6–12 m	3	3	0
Over 12 m	5	2	3
All	19	12	7

A





B





Fig 2 Right hip of a boy aged 13 at the time of nailing of the left hip 14 9 60
A — The epiphyseal line is regular except in the middle in the lateral view
B — Three months later after nailing of the other hip and bed rest the irregularity in the middle of the epiphyseal plate has disappeared and the position of the epiphysis is concentric

In 6 cases the interval between slipping in the first and in the second hip was less than 1 month and these were mainly cases in which both hips were operated on within a shor period In one case where the interval was 6 months the patient had been in consultation at our out patient department when right hip had a slip of 1/3 and the left merely a very slight slip An operation was not considered necessary and the patient was given crutches and allowed to move with their aid On the patient s re appearance after six months the slipping had increased, especially on the left side where it had been quite minimal at the earlier visit Moore pins were used for fixation on the left side The epiphyseal plate on the right was considered closed

Table 5 shows treatment received by patients elsewhere before coming to hospital

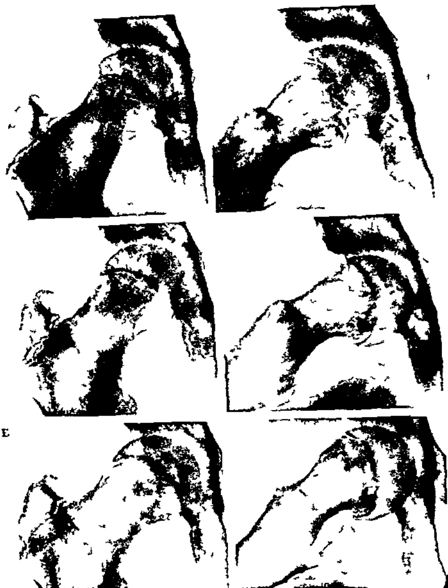


Fig. **C** Three months later. The epiphyseal line is more irregular in the lateral X-ray than in previous roentgenogram. The patient had no symptom. This X-ray was taken at the ... time as the ... lateral X-ray from the other nailed hip.
D ... months later there was a clear slip seen in the lateral X-ray. The irregularity of the epiphyseal line is also evident. The patient still felt no pain in this hip. In the antero-posterior X-ray the hump in the upper corner has disappeared, indicating a slip.
E Two months later. The slip is even more advanced. In the lateral view the protruding upper corner has been resorbed and a corresponding amount of secondary callus has formed in the lower part of the neck in the lateral view. The hip was nailed although the boy felt no pain in his hip ... of the slipping.

Table 5

Treatment before coming to hospital

Previous Treatment	Number of patients	Boys	Girls
No previous treatment	36	26	10
Incorrect diagnosis	17	12	5
Traction treatment	14	7	7
Rest in bed	8	6	2
Other treatment	2	1	1
Operative treatment	3	3	0
All	80	55	25

There were 17 cases of incorrect diagnosis elsewhere 4 of which were bilateral Ten of these patients had been treated on an incorrect diagnosis elsewhere, and 7 had received *no treatment before coming to hospital* One case had been considered a fracture One case had been mistaken for tuberculosis of the hip one for muscular paralysis and 2 had been treated for muscular sprain One was thought to be the result of excessive growth and not X rayed although there was pain in the hips On arrival at hospital slipping was under 1/3 on both sides In one case nothing was detected despite pain in the hip, but 2 weeks bed rest was prescribed slipping was less than 1/2 *In 3 cases the patient was treated as a Calve Legg-Perthes disease by Thomas* splint or rest In 36 cases the patient came straight to hospital without previous treatment with a correct diagnosis Other treatment given in this group consisted of Thomas splint in one case and crutches in an other Operative *treatment elsewhere consisted of one nailing* one wedge *osteotomy and one* attempted open reduction

Table 6 shows the age of patients on coming for treatment

Table 6

Age at time of operation

Age	Number of patients	Boys	Girls
Under 10 years	1	1	—
10—11 years	1	—	1
11—12 years	11	3	8
12—13 years	15	6	9
13—14 years	16	10	6
14—15 years	11	11	—
Over 15 years	25	24	1
All	80	55	25

At the time of operation the youngest patient was aged 9 years the oldest 37 years The last mentioned case had a residual stage of the slipped femoral epiphysis and an intertrochanteric osteotomy was performed Mean age of patients at the time of operation was 14 4 years Mean age of girls was 12 6 years and that of boys 15 2 years Six patients had sustained a trauma before admission to hospital In 4 of these cases the degree of slipping was less than half the extent of the epiphysis in one case over half and in one case the slipping was complete In the two latter cases a subcapital wedge osteotomy was performed and in one of the cases where the slipping was less than half the extent of the capital epiphysis an open reduction was performed The others were fixed by nailing or with bone pegs by Howorth s method

METHODS OF TREATMENT

Of the 80 patients in the present material 19 had a bilateral slip so that the total number of hips treated was therefore 99. The treatment given may be divided roughly into two main groups: conservative and operative. Table 7 shows the number of hips treated conservatively and operatively.

Table 7

Conservative and operative treatment

Degree of slipping	No Hips	Treatment operative	conservative
Slight	18	17	1
Under 1/3	26	22	4
Under 1/2	24	23	1
Over 1/2	29	25	4
Total	2	1	1
All	99	88	11

NON-OPERATIVE TREATMENT

Traction and closed reduction

In earlier years traction before operation was considered a routine treatment. In the later years it has not been practiced any more. Traction was mentioned as being used only in two cases in this material at our hospital and in 14 cases at another hospital.

Closed reduction was attempted under anaesthesia in 4 cases at another hospital before coming for treatment and in 6 cases closed reduction was attempted at our hospital. The capital epiphysis was fixed in all cases after manipulation. Only in 4 cases of these 10 manipulated cases was the position of the capital epiphysis considered better after closed reduction. All these

4 cases were those in which an obvious recent slipping had taken place In two cases the closed reduction was performed a few days after sudden exacerbation of pain in the hip in connection of a trauma Two cases were manipulated in a few weeks after such an accident

Conservative treatment

The conservative treatment group contains only 4 patients who actually received conservative treatment at our hospital Six patients had been treated elsewhere or had not been diagnosed and at the moment of consultation were unsuitable for any kind of treatment mostly because of closing of the epiphyseal plate

One of these was the case in which an open reduction had been attempted while the degree of slipping was less than half the extent of the capital epiphysis The operation was unsuccessful and resulted in a complete slipping which was not corrected The patient was sent to our hospital a few years after this operation and the epiphyseal plate was already closed and no further operation was considered indicated The result was later regarded as poor

In 3 cases the patient had been treated for an incorrect diagnosis or the slipping had not been diagnosed One of these had been treated for tuberculosis of the hip for one year with bed rest The degree of slipping was slight and as the epiphyseal plate had already closed there was no indication for further treatment The result was good In one further case the patient had pain in the hip but no radiological examination had been performed The degree of slipping was in this case more than half the extent of the capital epiphysis and as the epiphyseal plate had closed in this case too no treatment was considered necessary The hip was stiff at the time of follow up The third case with an incorrect diagnosis had received no treatment This was a bilateral slipping in which both epiphyseal plates had closed on arrival at the hospital One hip was left uncorrected but in the other a sub trochanteric osteotomy was performed Three further cases were bilateral cases in which one hip had already stabilised so that no treatment was given The other hips were treated as follows nailing was performed in one case open reduction was attempted in one case wedge osteotomy was performed in one case

Only four patients were given actual conservative treatment in one case a Thomas splint was used in another closed reduction was attempted and the hip immobilised in plaster for a month and in two cases the patient was

allowed to move with elbow crutches The fourth case had attended the out patient department of our hospital, when a slip of 1/3 was found in one hip and merely a very slight slip in the other *As previously mentioned operative* treatment was not considered necessary and the patient was allowed to move with elbow crutches, but when he reappeared at the hospital six months later the slipping had greatly increased especially on the left side, where there was previously only a brightness of the epiphyseal line The slipping was less than 1/3 on both sides The left side was then considered so acute that it was fixed with Moore pins, but on the right side the epiphyseal line was considered to have closed The slip had not increased in this hip

OPERATIVE TREATMENT

Table 8 shows to what extent various operative methods were used in varying degrees of slipping

Table 8

Operative methods

Type of operation	No Hips	Degree of slipping: Slight	Under 1/3	Under 1/2	Over 1/2	Complete
Nailing	51	17	20	12	2	—
Howorth	15	—	2	5	8	—
Wedge ost	9	—	—	2	6	1
Intertr or subtr ost	7	—	—	2	5	—
Open reduction	4	—	—	2	2	—
Other oper	2	—	—	—	2	—
All	88	17	22	23	25	1

In earlier years an ordinary Smith Petersen or vitallium nail was used but in the last few years these have been replaced by smaller nails intended for children Fixation by nailing without reduction was generally performed when the slipping was less than half the extent of the epiphysis Intertrochan teric and subtrochanteric osteotomy was performed in order to correct posi tion, mainly in the residual stage of the slipping Other operations consisted of Judet arthoplasty performed after an unsuccesful open reduction in the other case a drilling operation was performed In recent years nailing and

Howorth operation have become more common at our hospital, while wedge osteotomy and open reduction are no longer performed

After nailing no post operative plaster was used Routine treatment after nailing was a follows during the first 10 days the patient was allowed to get up and use elbow crutches he was allowed full weight bearing on the operated limb only after 2—3 months In the present material 33 patients were in bed for less than one month after nailing also less than a month in bed were 12 patients after Howorth operation one wedge osteotomy one open reduction and one drilling operation The other patients were more than a month in bed most had been operated in previous years when the immobilisation time was longer

FOLLOW UP EXAMINATION

The follow up examination was performed in 1967 The number of patients appearing at the examination was 79 19 were bilateral so that the total number of hips was 98 One patient had died of brain tumor 2 years after operation The shortest period of observation was one year and the longest 19 years with a mean of 6 7 years The youngest patient at follow up was 13 years and the oldest 40 years with a mean age of 21 6 years

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Other oper	2	—	—	—	2	—
All	88	17	22	23	25	1

In earlier years an ordinary Smith Petersen or vitallium nail was used but in the last few years these have been replaced by smaller nails intended for children Fixation by nailing without reduction was generally performed when the slipping was less than half the extent of the epiphysis Intertrochanteric and subtrochanteric osteotomy was performed in order to correct position mainly in the residual stage of the slipping Other operations consisted of Judet arthoplasty, performed after an unsuccesful open reduction in the other case a drilling operation was performed In recent years nailing and

The result was considered excellent when the Gade mobility index was 85 or more In these cases the X ray showed a virtually normal hip and the patient felt no discomfort In unilateral cases the result was compared with the normal hip Mobility then had to be at most 10 points under the value estimated for the normal hip

The result was considered good when the Gade mobility index was 75—85 The patient might have slight pain after strain and the X ray might show slight changes In order to simplify the comparison of results the excellent and good cases are grouped together in the tables

The result was considered fair if the mobility index was 50—75 The patient felt pain after strain and the X ray showed moderate changes in the joint surfaces

The result was considered poor if mobility was 50 or less In such cases the X ray showed marked changes and the patient might feel pain even after slight strain In the present material no patient felt sufficient pain to incapacitate him completely The highest Gade index obtained for a healthy hip in this series was 91

NON OPERATIVE TREATMENT

Traction

Traction was used in 14 cases at another hospital before coming for treatment and in two cases in this hospital

In those 14 patients treated with traction elsewhere the degree of slipping was slight in one case under 1/3 in 3 cases under 1/2 in 3 cases and over 1/2 in seven cases (Table 10) Of those patients treated with traction at our hospital the degree of slipping was under 1/3 in one case and complete in one case The table 10 shows the result of different types of treatment after pre-operative traction

In those cases where the result of traction could be controlled it had not changed the position of the epiphysis As can be seen in Table 10 the results of treatment according to degree of slipping are approximately the same as in the rest of the series (Tables 10 and 17) This means that the traction had not much influenced the result of treatment

After preoperative traction the epiphysis was fixed in seven cases according to Howorth in five cases a simple nailing was performed and in two cases a wedge osteotomy was performed after which the capital epiphysis was fixed by Smith Petersen nail In one case an arthroplasty was performed

RESULTS

Assessment of results

Results were assessed by clinical examination of patients. Particular attention was paid to the patient's own estimation of the result, pains felt at rest or under strain, ability to work, and the patient's opinion in general. Secondly the degree of mobility of the hip was assessed by clinical examination and expressed according to Gade. Thirdly X-ray examination was carried out, with exposures taken in the antero-posterior and lateral or so called Lauenstein positions in all cases.

Table 9

Assessment of Results

	Patient's estimation	Pain	Function	Movement index (Gade)	Radiographic appearance of hip
Excellent	Normal	None	Unrestricted	85 or over	Virtually normal hip, viable head good joint space
Good	Good hip, not quite normal	Does not interfere	Slightly restricted	75—85	Concruent surfaces viable head good joint space
Fair	Some trouble	Stops some activities	Definitely restricted	50—75	Some irregularity slipping of head narrowed joint space
Poor	In some cases troublesome	Partly disabling	Poor	Under 50	Joint space lost or necrosis of head

Table 11

Results of treatment after preoperative closed reduction

Degree of slipping	No	Results: Excellent or good	Fair	Poor
Slight	0	0	0	0
Under 1/3	1	0	1	0
Under 1/2	4	1	2	1
Over 1/2	5	1	2	2
Complete	0	0	0	0
All	10	2	5	3

As the table shows the results are no better than in the rest of the series and in some respects they are probably worse (Table 11 and 17)

The result at the time of follow up in those four cases in which the position was regarded as better after manipulation was good in one case fair in two cases and poor in one case The distribution of results according to the degree of slipping is thus somewhat worse than in the rest of the material As the number of cases of closed reductions is very small no accurate conclusions can be made but in this group there were more poor cases than in the whole material The method of fixing the epiphysis after manipulation in the poor cases was nailing in one case (Fig 3) and Howorth operation in one case The third case was manipulated first after which an open reduction was attempted and the head later replaced by the Judet prothesis An arthrodesis was performed at another hospital later In the first two cases a necrosis of the femoral head resulted with stiffening of the joint

It seems therefore that the result of an attempted closed reduction is uncertain and contains a considerable risk of necrosis of the femoral head If it is attempted it must preferably be done in a very recent slipping

Conservative treatment

The group in which the treatment was considered as conservative because no operations were performed contained two cases considered as poor at follow up In one of these an open reduction had been attempted at another hospital The patient came for consultation a few years later when the epiphyseal plate had already closed the joint was stiff and no further operations

Table 10

Results in cases of preoperative traction

Degree of slipping	No	Results Excellent or good	Fair	Poor
Slight	1	1	0	0
Under 1/3	4	3	1	0
Under 1/2	3	3	0	0
Over 1/2	7	5	0	2
Complete	1	0	1	0
All	16	12	2	2

The degree of slipping in the hips operated according to Howorth was over half of the extent of the epiphysis in five cases, under half in one case and under a third in one case In one of these cases the result of treatment at the time of follow up was considered as poor, the other as excellent or good

The degree of slipping in the cases in which a wedge osteotomy was perfomed was over half in one case and complete in one Both cases were considered as good at the time of follow up In those fixed by nailing the degree of slip ping was slight in one case, under 1/3 in two and under 1/2 in two cases They were all considered as good at the time of follow up In two cases a closed reduction was attempted after a traction treatment at another hospital The position of the head improved

Closed reduction

In 4 cases in this series a closed reduction was attempted at another hospital In six further cases a closed reduct on was performed at our hospital Only in four of these ten cases was the position of the capital epiphysis regarded as better by the surgeon after manipulation These four cases were all recent slippings in which the closed reduction was attempted in a few days after accident in two cases however a few weeks Fig 3 shows one case in which the position was regarded as better after a closed reduction but in which a necrosis of the head resulted

Table 11 shows the results of different types of treatment after preoperative closed reduction



Fig 3 C. A th s was a very recent *case a closed red* cu n was performed and the ep *physis* fixed by n l ng Th pos ti n f the h ad *is ery good indeed* The na l is in a good posit on
D. A necros of the epipl ysis developed in the middle of the epiphy is 8 months later and he *na l had t be* removed exa tly a year *after* na l ng *However* the necrosis of *the head* r ased
E. Eight ars aft n ling the fem al head was qu te irregular and the h p was stiff A d trochi ter steot ny was performed at another h spital *and at the foll* w up ten years aft r nail ng th l ade *n3ex I* the *right h* p was 5C and *8o for the left* hip which was also n ilex The result *n the right* h p was regarded as poor because cf the appearance *in the* X ray Th wa the on l *poor result* among 51 *nail ngs*

A





B





Fig 3 Right hip of a girl aged 12 at the time of nailing and closed reduction
A — The patient felt pain in the right hip and an X ray was taken at another hospital in both positions No signs of a slip was seen *and the patient* was sent home *In the lateral X ray* a slight slip is clearly visible
B — The patient had fallen two days after the previous X ray was taken and the pain in the right hip became worse In a new X ra a market slip was seen and the patient was admitted to the hospital for nailing

were indicated The other was a neglected case in which the degree of slipping was more than half the extent of the epiphysis This had not been diagnosed On arrival at the hospital the epiphyseal plate had closed The Gade mobility index was 12 in the first case and 46 in the other

Table 13

Results by nailing

Degree of slipping	No Hips	Results Excellent or good	Fair	Poor
Slight	17	17	—	—
Under 1/3	19	16	3	—
Under 1/2	11	10	1	—
Over 1/2	3	1	1	1
Complete	—	—	—	—
All	50	44	5	1

When a Smith Petersen or vitallium nail is used the literature records cases in which the nail pushes the capital epiphysis forward before the nail It is also possible that a thick nail may split the epiphysis In the present material complications of this type did not occur in a single case (Figs 4–6) In 3 cases however the nail was driven too far and penetrated the joint cartilage of the epiphysis In only one case was necrosis of the epiphysis observed at follow up examination (Fig 3) A closed reduction had been performed in connection with nailing In this case the caput had slipped about half the extent and closed reduction was performed during the operation The patient felt no subjective discomfort worth mentioning The Cade mobility index was 56 but because of changes in the X ray the condition as a whole was considered poor (Fig 3) In the 3 cases in which the nail had penetrated the joint cartilage no signs of this could be seen in the follow up X rays

In 2 cases the nail came out and the patient had to be operated again In one of these cases one month had elapsed since the operation and in the other case 5 months In the latter the slipped epiphysis was bilateral and the nail came out on both sides it therefore had to be driven in again several months later In one case it was observed that the nail did not fix the epiphysis and the patient was re-operated 6 weeks after the first operation

In only one case were Moore pins used In this case a postoperative X ray control showed that these were placed in the dorsal part of the femoral neck where they did not fix the epiphysis It was therefore necessary to remove them five weeks after operation The condition healed nevertheless with a good result

Table 12 shows the results at the time of follow up examination in cases in which no operations were performed

Table 12

Results of conservative treatment

		Results		
Degree of slipping	No	Excellent or good	Fair	Poor
Slight	*1*	*1*	*0*	*0*
Under 1/3	4	2	2	0
Under 1/2	*1*	*0*	*1*	*0*
Over 1/2	4	1	2	1
Complete	1	0	0	1
All	11	4	5	2

Three of these patients were treated elsewhere either by traction, imm bilisation in plaster or immobilisation in bed The result was excellent i one case, fair in two

One patient was treated by immobilisation in plaster at our hospital Th result was fair The others were allowed to move either with elbow crutche or with a Thomas Splint

The conservative treatment was used in earlier years The number of thes cases is so small that no conclusions can be drawn It looks as if the distribu tion of results was the same as in the rest of the material depending on th degree of slipping As at least one of these patients had become worse an the degree of slip had increased during walking with elbow crutches it i obvious that fixing the epiphysis at an early stage diminishes the risk of fur ther slipping and a poorer result A conservative treatment seems therefor to be seldom justified

OPERATIVE TREATMENT

Results by nailing

Table 13 shows the result of treatment according to degree of slipping in cases where the capital *epiphysis was fixed by nailing*



Fig. 5 Left hip of a girl aged 11 at the time of nailing.
A. The degree of slipping was considered to be less than half of the extent of the epiphysis. The lateral view on the right.
B. The epiphysis was fixed with a vitallium nail without an attempt at closed reduction. Closed reduction had been attempted at another hospital previously without success. This X-ray was taken 3 months after nailing and as can be seen in the lateral view the protruding part of the neck in its upper corner has resorbed.
C. At the follow-up 3½ years after operation the hip movements were free except for the slight restriction of the internal rotation. No discomfort. No limp. Index of mobility according [illegible] was over 85. The result was considered excellent.

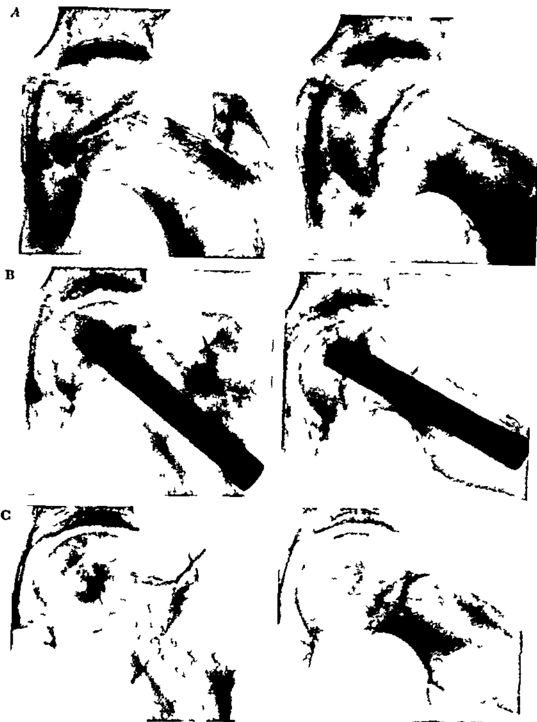


Fig 4 *Left hip* of a boy aged 14 at the time of nailing. This is the same case as in Fig 1
A — The degree of slipping was regarded as slight and the capital epiphysis fixed with a *vitallium nail*
B — Two months after nailing
C — Six years 3 months after operation at the follow up examination. The patient had done his military service. No pains in limb. No discrepancy of the legs. The Cade index over 85 in both hip. The result was regarded as excellent

Howorth s operation

The Howorth operation or bone pegging has been practised at our hospital since 1961 Up to the end of 1965 a total of 15 operations according to this method had been performed The number is now somewhat higher The indication for this kind of fixing of the epiphysis has been a slipping of at least 1/3 of the extent of the capital epiphysis usually more The operation is in our opinion simple and easy to perform. The postoperative mobilisation of the patient is quick The patients have been allowed to move with elbow crutches in 2 -3 weeks after operation without weight bearing and full weight bearing is allowed according to signs of closure of the epiphyseal plate in the X ray This has usually been in 2—3 months postoperatively The passive and active joint movements are begun during the first postoperative week (Figs 7 and 8)

Table 14 shows the results of Howorth operation at the time of follow up examination according to the degree of slipping

Table 14

Results with Howorth operation

		Results		
Degree of slipping	No	Excellent or good	Fair	Poor
Slight	0	0	0	0
Under 1/3	2	2	0	0
Under 1/2	5	2	2	1
Over 1/2	8	7	0	1
Complete	0	0	0	0
All	15	11	2	2

In one case regarded as poor at the follow up a closed reduction had been attempted previously at another hospital without result The degree of slip was under 1/2 but was mostly backwards so that the position of the leg was in external rotation Possibly a subtrochanteric correction osteotomy should have been indicated This was no performed however At the follow up almost 4 years after operation the movements of the hip were the same as before the operation except for rotations which were absent The patient had no symptoms but in the X ray a slight arthrosis was evident The Gade mobility index was 45

A





B





C





Fig 6 Left hip of a girl aged 12 at the time of nailing

A — The degree of slipping was considered as less than half of the extent of the epiphysis

The slipping can be seen in the antero-posterior X ray too

B — The epiphysis was fixed with a Smith Petersen nail The X ray was taken two months postoperatively

C — Nine years after operation No discomfort Plays tennis and other sports like skiing and swimming No limp No discrepancy of the legs Index of motion according to Gade 85 The result was regarded as excellent



Fig 8 The left hip of a girl aged 12 at the time of Howorth operation.

A The degree of slip was regarded as over half of the extent of the epiphysis. The internal rotation was absent before operation.

B Three months after Howorth operation. The bone pegs are clearly seen.

C. Four years 7 months postoperatively. No discomfort. Works in a shop as a salesgirl. No limp. No discrepancy. All movements are free including the internal rotation. Gade index 85. The result was regarded as excellent.

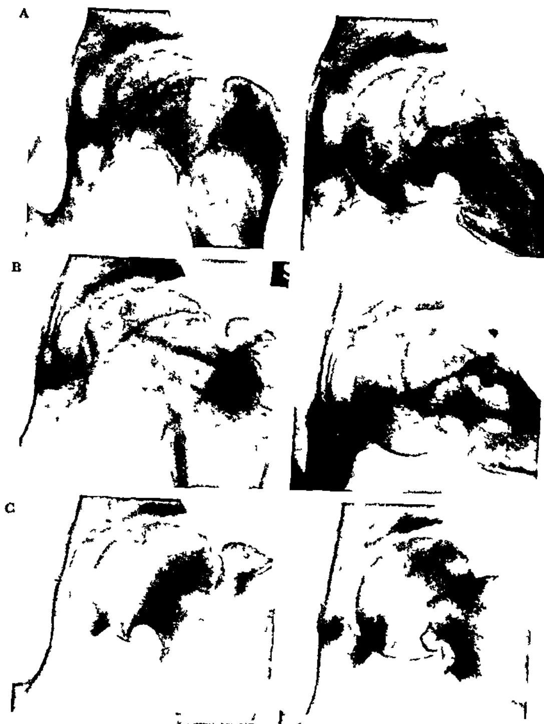


Fig 7 Left hip of a boy aged 13 at the time of Howorth operation
A – The degree of slip was regarded as less than third of the extent of the epiphysis Adduction and internal rotation were limited before operation The left leg was 1 cm shorter than the right
B – 3½ months after bone pegging operation according to Howorth
C – 2 years and 5 months after operation at follow up No discomfort The internal rotation limited Walks without limp The index of motion 77.5 The result was regarded as good

Table 15

Results with wedge osteotomy

Degree of slipping	No	Results Excellent or good	Fair	Poor
Slight	0	0	0	0
Under 1/3	0	0	0	0
Under 1/2	2	2	0	0
Over 1/2	6	6	0	0
Complete	1	0	1	0
Total	9	8	1	0

All these osteotomies were performed between 1957—1960 As reports by different authors were less encouraging they have not been performed since As can be seen in Table 15 the results at the follow up in this small group of wedge osteotomies are surprisingly good and correspond to results reported recently by Dunn (1964) and others (Figs 9 10 and 11) It is unlikely however that an osteotomy of the neck should be indicated in cases where the degree of slipping is small as the results without such an osteotomy in these cases are excellent or good even in this material

Open reduction

Open reduction here means an operative *repositioning* of the epiphysis of the femoral head without resection of the neck

The open reductions were performed in 1954—1963 and they were four in all

After open reduction the femoral head was fixed *with* McLaughlin nail in two cases with Smith Petersen nail in one case and was *left* without internal fixation in one case Plaster immobilisation was used in two cases

One case was regarded as excellent at follow up 11 years after operation The Gade mobility index in this case was over 85 The patient had been classified as a Grade A *during the military* service He had no symptoms no limp no discrepancy The radiologic appearence of the head was good

The result in two cases was regarded as good The Gade mobility index was 81 in one patient and 75 in the other They had no symptoms One of them came to follow up 13 years after operation the other 6 years after operation Despite the lack of symptoms they were not accepted for military service The head was slightly deformed in both cases in the X ray (Fig 12)

In the other case regarded as poor there was nothing exceptional The degree of slip was over 1/2 The patient was 4 weeks in bed postoperatively and began full weight bearing in 4 months Later a subtrochanteric osteotomy was regarded as indicated for varus external rotation deformity, but for some reason this was not performed Obviously this would not have improved the mobility, which poor was very already preoperatively There were only 30 degrees of flexion while other movements were absent At the follow up only 15 degrees of flexion were observed The Gade mobility index was 9 The patient had no symptoms In the X ray of the hip there was a superficial necrosis of the femoral head and acetabulum similar to the so called Waldenstrom's disease In both cases regarded as poor no obvious reason for this was observed at the operation itself

In one case regarded as fair at the follow up an attempt of closed reduction was made during the operation The position of the head could not be changed however In a postoperative X ray one tibial graft was observed to have penetrated the surface of the femoral head into the joint At the follow up 5 years after operation the femoral head was deformed in the X ray but the tibial grafts had resorbed

In both cases regarded as fair a subtrochanteric osteotomy was performed The Gade mobility index was 61 in one case and 66 in the other The latter was a patient with a pituitary tumour His height at the follow up was 218 cm He was treated by radiotherapy before orthopedic operations

As our indications for Howorth operation have occurred in patients with more advanced slippings the results can be regarded as good in our opinion (Figs 7, 8)

Wedge osteotomy

In nine cases in this material a wedge osteotomy of the femoral neck was performed The wedge was taken from the middle of the neck with its base in the upper anterior part so that the varus external rotation deformity could be corrected In five cases a postoperative immobilisation in a plaster hip spica for from 6 to 8 weeks was used The fragments were fixed in all cases with a Smith Petersen nail In one case the nail came out of the neck after 4 weeks and the patient had to be operated again An intertrochanteric correction osteotomy was done at the same time as refixation of the fragments The result in this case was excellent six years later at the follow up

The results at the follow up according to the degree of slipping are shown in Table 15

Table 15

Results with wedge osteotomy

Degree of slipping	No	Results Excellent or good	Fair	Poor
Slight	0	0	0	0
Under 1/3	0	0	0	0
Under 1/2	2	2	0	0
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Complete	1	0	1	0
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The results at the follow up according to the degree of slipping are shown in Table 15



Fig. 10. The left hip of a girl aged 14 at the time of a wedge osteotomy.
A. The degree of slip was estimated as over half of the extent of the epiphysis. Rotations and abduction were absent before operation. The left extremity was 2½ cm shorter.
B. A few weeks after a wedge osteotomy and fixation with a Smith Petersen nail.
C. Eighteen [illegible] 5 months after operation. Walks almost without a limp. The left leg is 1½ [illegible] cm short. The internal rotation is limited, otherwise hip movements are free. No discomfort. Index of mobility 85. The result was regarded as excellent.

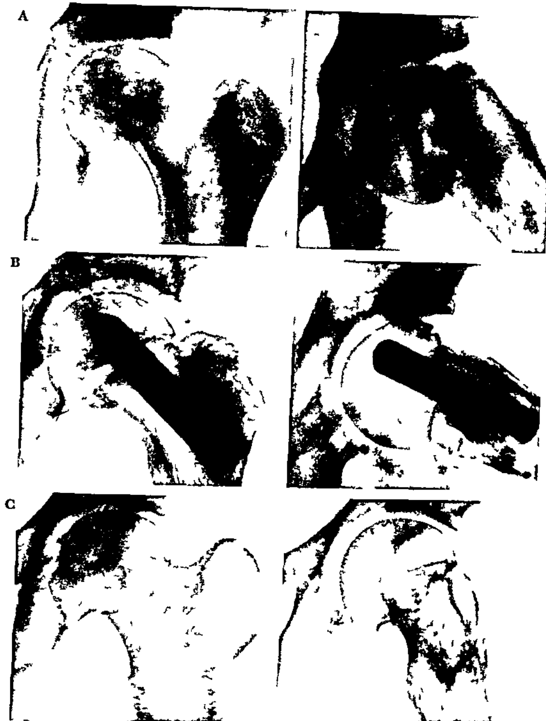


Fig 9 *The left hip of a boy aged 14 at the time of a wedge osteotomy*
A — The degree of slip was regarded as over half of the extent of the epiphysis The boy felt pain in the hip for 6 months
B — One month after a wedge osteotomy The fragments were fixed with a Smith Petersen nail and a plaster hip spica was applied for a month
C — Nine years 6 months postoperatively No discomfort Slight limp The left leg is 2 cm shorter Except for internal rotation the hip movements are free Index of mobility 77 Result was considered good

The result in one case was regarded as poor at the follow up In this case the fragments were fixed with a McLaughlin nail which obviously penetrated the surface of the femoral head into the joint This was evident in the special control X rays after operation The nail was left in place however and re sulted in cartilage necrosis of the femoral head At the follow up 4 years after operation the patient felt pains on strain The Gade mobility index was 54 but because of the appearance in the X ray the result was regarded as poor (Fig 13)

Thus the results in three of four cases were excellent or good after 6—13 years follow up Only one result was regarded as poor and even in this case the reason for a poor result was not the open reduction itself but a nail pen etrating the joint cartilage The number of operations is so small however that no further conclusions can be made according to the value of this oper ation or the risk involved

ALL TYPES OF TREATMENT

The result with all types of treatment summarised are shown in Table 16

Table 16

Results with different types of treatment

Treatment	No Hips	Results: Excellent or good	Fair	Poor
Nailing	50	44	5	1
Howorth oper	15	11	2	2
Wedge ost	9	8	1	—
Open reduct	4	3	—	1
Other oper	9	1	7	1
Cons treat	11	4	5	2
All	98	71	20	7

The group other operations contains 7 subtrochanteric and intertro chanteric osteotomies one drilling operation and the previously mentioned Judet arthroplasty after an unsuccessful open reduction In the present ma terial 5 other intertrochanteric or subtrochanteric osteotomies were perfor med after nailing or Howorth operation These have not been mentioned separately however The Judet arthroplasty led to a poor result It was per formed as mentioned in connection with an unsuccessful attempt at open reduction and the arthroplasty itself produced a painful condition later

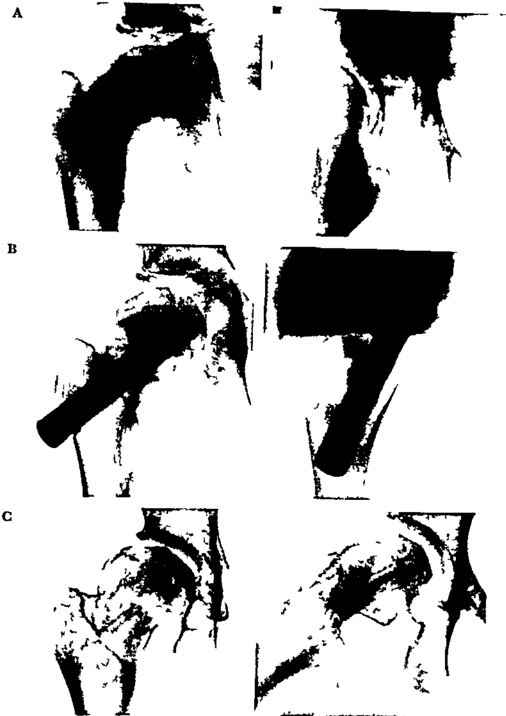


Fig 11 Right hip of a girl aged 11 at the time of a wedge osteotomy

A – The degree of slip was complete Traction was applied for one month without effect

B – One week after a wedge osteotomy and fixation with a vitallium nail A slight necrosis of the epiphysis was noticed t ... after operation and a Thomas splint was used The nail was removed two years r r n

C – Seven years after operation No discomfort Walks with a slight limp No discrepancy of the legs The r ... r are restricted Grade index 70 The result was regarded as fair

The result in one case was regarded as poor at the follow up In this case the fragments were fixed with a McLaughlin nail which obviously penetrated the su face of the f moral head into the joint This was evident in the special control X rays after operation The nail was left in place however and re sulted in cartilage necrosis of the femoral head At the follow up 4 years after operation the patient felt pains on strain The Gade mobility index was 54 but because of the appearance in the X ray the result was regarded as poor (Fig 13)

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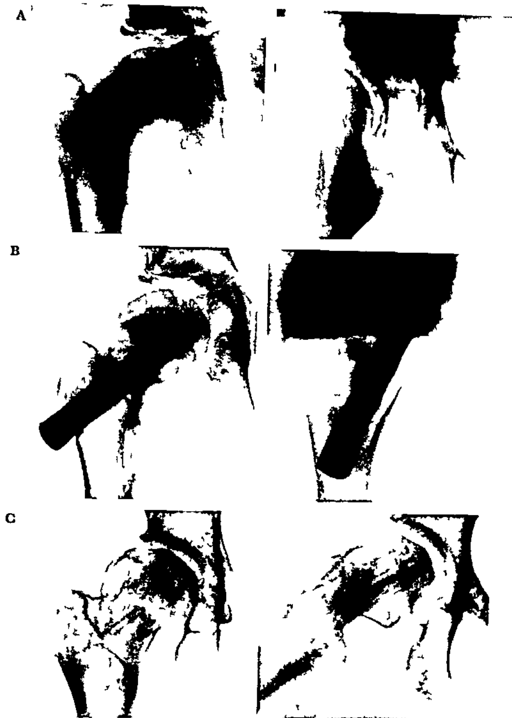


Fig 11 Right hip of a girl aged 11 at the time of a wedge osteotomy
A – The degree of slip was complete Traction was applied for one month without effect
B – One week after a c steotomy and fixation with a vitallium nail A slight necrosis of the ep physis was noticed a few months after operation and a Thomas splint was used The nail was removed two years after operation
C – Seven years after operation No discomfort Walks with a slight limp No discrepancy of the legs The rotations are restricted Gade index 70 The result was regarded as fair

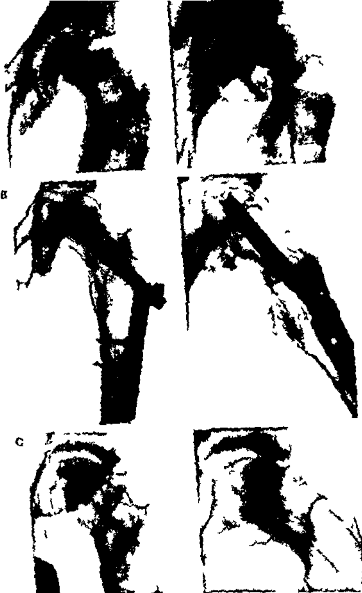


Fig 13 Th l ft h p f boy aged 1f at th time of an open red ct n.
A Th degree f l p wa over half of the e tent of the epiphys s. All h p movements were m ted
B Thr week after an open reduct on and fixat n w th a McLaughlin na l The nail wem be n pla bt t n tangential X ray it was seen to penetrate the joint surface of the f h a A th pat ent d l n t ha e an symptoms the na l was left in place for four months an l then removed
C At he f ll w up three years 9 months postoperat ely The pat ent f lt pain in the hip fter walk ng Walk w th a l mp The left lower xtrem ty is l cm sh rt The rotations are absent Ab lu t on and ad lu t on 10 – 15 degrees Gade in lex 54 S gns of cartilage necrosis th X y a n l t the so-called Waldenström s disease Th result was regarded as poor

A



B



C



Fig 12 The right hip of a boy aged 15 at the time of open reduction and an intertrochanteric osteotomy

A — The degree of slip was over half of the extent of the epiphysis

B — One month after an open reduction and an intertrochanteric osteotomy Plaster hip spica was used for one month The fragments were fixed with a McLaughlin nail

C — Seven years after operation No discomfort Walks with a slight limp The right lower extremity is 1 cm shorter The index of motion is 81 The result was regarded as good

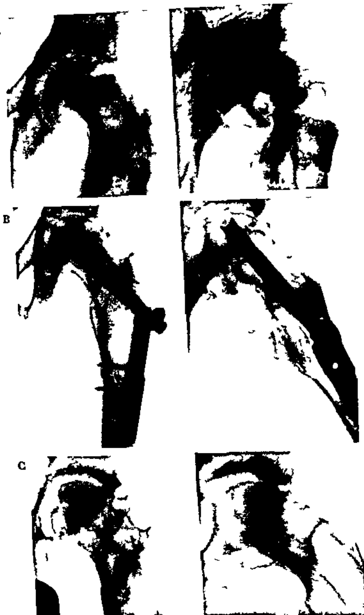


Fig 13 Th l ft h p of a bo ged 16 at th time of an open reduction
A – The degree of lip was over half of the ext nt of the ep phys s All h p movements were restricted
B – Three weeks after an open reduction and fixat on with a McLaughlin na l. The nail seem to be n place but in tangential X ay it was seen to penet ate the jo nt surface of the ep physis As the pat ent d d not ha e a y symptoms the nail was left in place for four months nd then emo ed
C. – At the follow up th ee years 8 months postoperat ely The patient felt pain in the hip after walking Walks w th a l mp The left lower ext emity is 1 cm short. The rotations are absent. Abdu tion and adduct on 10—15 degrees Gade index 54 S gns of cartilage necrosis in th X ray sim lar to the so-called W ldenstrom s desease The result was regarded as poor

A





B





C





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DISCUSSION

The etiology of the slipped upper femoral epiphysis is quite evidently connected with hormonal influence at least in some respect. Roughly 30 per cent of the patients in this material were overweight or even more clearly had an endocrine disturbance. As Harris (1950) observed an excess of the growth hormone may weaken the epiphyseal plate and the sex hormone strengthens it against tangential strain. The tallest boy in this material was 218 cm or 7 ft 3 ins. It is naturally of some importance that not all cases of slipped epiphysis are bilateral. On the other hand the diagnosis of very slight slip which may recover without treatment is very difficult. Using a careful and thorough technique of examination Billing and Severin (1959) found evidence of a bilateral slip in 80 per cent of cases. A mere weakening of the epiphyseal plate without displacement may even then escape diagnosis (Figs. 1, 2.) Thus a very high percentage of cases are after all bilateral.

If a lateral radiograph is taken the diagnosis of a slipped femoral epiphysis is in most cases easy. This is often neglected however and in an anteroposterior radiograph a slight slip can only be diagnosed with difficulty despite the typical signs described by Jerre (1950) and Waldenstrom (1939).

Howorth (1966) has stated that there exists a so-called preslipping stage in which there is only swelling of the synovial membrane and villous formation. In this material there were 11 hips in which the only sign of a slip was widening or irregularity of the epiphyseal line in the lateral X ray or a slip of 1 - 2 mm only. Six of these patients felt pains in the hip but five did not. Thus obviously a preslipping stage may exist without symptoms.

Traction did not seem to affect the result of treatment in this material. Its use has therefore been abandoned at our hospital in the preoperative treatment of a slipped epiphysis.

Closed reduction was successful in four cases out of ten in this material. Of these four cases in which the closed reduction was considered to have improved the position of the head only one was regarded as good at the follow up. One was poor and two fair. It seems to us that a closed reduction

Denervation was carried out later, but brought no relief Eventually arthrodesis was performed at another hospital The result was naturally considered poor In the two conservative cases with poor results, the patient on whom operative reduction had been attempted elsewhere came for follow up examination 6 years after the original operation without the slighest discomfort There was a 5 cm shortening of the lower limb, the Gade mobility index was 12, and the X ray picture showed that the capital epiphysis had almost disappeared The other patient came for follow up 9 years after the original visit There had been a slipping of over half the extent of the epiphysis He had advanced stiffness in the hip The X ray showed that the head was completely deformed The Gade index was 46 The result was considered poor

As shown earlier in the literature the extent of slipping has an important effect on results Table 17 therefore shows the whole material classified according to degree of slipping, irrespective of treatment

Table 17

Result with all types of treatment according to displacement

		Results		
Degree of slipping	*No Hips*	*Excellent or good*	*Fair*	*Poor*
Slight	18	18	—	—
Under 1/3	25	20	5	—
Under 1/2	24	16	7	1
Over 1/2	29	17	7	5
Complete	2	—	1	1
All	98	71	20	7

Although operations in this series have been performed by several different methods and by different surgeons over a period of 20 years and although some cases have remained untreated because of neglect or incorrect diagnosis or have been treated conservatively it appears that the extent of slipping has a vital influence on results Thus in cases which have been considered satisfactory or poor at follow up slipping has usually been half or more than half the extent of the capital epiphysis This is natural because deformity resulting from considerable slipping and disturbance in development of the femoral head obviously has an adverse effect on the result regardless of treatment

DISCUSSION

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SUMMARY

The authors have analysed a total of 99 treated hips with a slipped femoral epiphysis of which 98 were re-examined at follow-up. The average observation time was 6.7 years. The longest observation time was 19 years. There were 19 bilateral cases. The degree of slipping was assessed from a lateral X-ray. Slipping was classified as slight, under 1/3, under 1/2, over 1/2 and complete slipping.

Fifty-one hips were treated by nailing and 50 of these patients appeared for follow-up. Fifteen hips were treated by Howorth's bone pegging operation, 9 by wedge osteotomy, 4 by open reduction, 7 by intertrochanteric or subtrochanteric osteotomy. One was treated by Judet arthroplasty and one by drilling. Eleven cases were treated conservatively, i.e. no operation was performed. Actual conservative treatment was given to 4 patients only. The remainder had been operated on in other hospitals or neglected.

Results were assessed from the patient's own estimation, from clinical examination and from X-rays. In clinical examination the Gade index was used. An index of 50 or less was considered poor.

At follow-up examination of the 50 nailed cases 44 were excellent or good, 5 fair and only one was poor. Of those 15 operated by the Howorth method 11 were excellent or good, 2 fair and 2 poor. After wedge osteotomy 8 cases were good or excellent, one was fair and none poor. After open reduction 3 were excellent or good, one was poor. The present material showed that the extent of the slipping had a marked effect on the result of treatment: when the slipping was less than half the extent of the epiphysis excellent or good results were achieved in 54 cases of 67 (80.6 per cent), fair in 12 (17.9 per cent) and poor in only one (1.5 per cent) regardless of the type of treatment or the method of operation. When the slipping was over half, however, 17 cases out of 31 (54.8 per cent) were excellent or good, 8 fair (25.8 per cent) and 6 poor (19.4 per cent). In the whole material 71 cases out of 98 (72.5 per cent) were excellent or good, 20 fair (20.4 per cent) and 7 poor (7.1 per cent).

is only indicated, if the slip is very recent and the degree of slipping is at least half the extent of the capital epiphysis, since results by nailing or Howorth operation without reduction are reasonably good in mild cases On the other hand, if the slipping is severe or complete the position of the head should be corrected either by closed reduction or better still with a wedge osteotomy

The number of cases of open reductions and wedge osteotomies is very small so that absolute conclusions cannot be drawn from the results obtained It seems, however, as if a wedge osteotomy might have a place in the treatment of a severe slip if the operation can be performed by a skilled surgeon

The Howorth operation was regarded as an easy and safe procedure The result in two cases regarded as poor at the follow up may result from other causes than the operation method itself, probably too wide an exposure at operation In most cases operated according to Howorth the degree of slipping was more than half the extent of the capital epiphysis, and this of course affects the result

The results by nailing with a Smith Petersen nail in this series are mostly good Complications that might occur with a trifin nail were observed only in very few cases and recovered without treatment in most of them Only one case in 50 was regarded as poor at the follow up, and in this case a closed reduction had also been performed In recent years we have used only thin nails intended for children The only complication that occurred was that the nail reached too far and penetrated the joint cartilage This of course can be prevented with proper operation technique and with a careful X ray control

Follow up examination showed that the fixation of the epiphysis is indicated in cases of slight and moderate slipping because its neglect may allow an increase of slipping later and affect the result adversely In the entire material the results were much better with any type of treatment in cases of slight or moderate slip The more severe the slip the less favorable is the result Therefore an early diagnosis of a slipped upper femoral epiphysis is the surest guarantee of a good result, as it is in the treatment of many other conditions in medical practice

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SUPPLEMENTUM 113

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by

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Translated from the Swedish

by

GRETA SARGEANT

Tryckeri Balder AB Stockholm 1968

To Monna

Contents

Preface

Achilles heel — the athlete s vulnerable spot — gave the impulse to this investigation

Curt Franksson inspired criticized and set the pace from start to finish

Lennart Widen encouraged me and provided facilities for the neuro physiological examinations

Anders Persson carried out the electromyographic examinations and analysed these and the operative findings

Erik Lindgren interpreted the X ray findings

Hans Nordenstam analysed the histological material

Torgny Sjostrand encouraged and supported the work

Stefan Jacobson s Elin Kopman s and Bertil Wallerman s photographic skill lent colour and shape to the work

Lars Glasser s old Dalecarlian country house provided an inspiring and peaceful working place

The investigation was supported financially by Folksam Insurance Company and the Poliklinikkommitten of the Swedish Sports Federation

Thus it was possible to carry out the work reported in the following

Introduction

Subcutaneous partial rupture of the Achilles tendon has been regarded as an uncommon injury (see the following) In a short period of time however the author has diagnosed this condition relatively often The object of this investigation was to throw light on the nature of the injury and to present a new method (by electromyography) for diagnosing the condition

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Definition

Subcutaneous partial rupture of the Achilles tendon refers here to a tear involving a varying number of fibres in the free portion of the Achilles tendon, usually leaving most fibres intact To distinguish clinically a partial rupture from a complete rupture is not difficult, because plantar flexion of the foot does not occur on Thompson's test (1960) — manual *compression of the triceps surae belly* — *if the rupture is complete* Absence of this reflex is pathognomonic for complete rupture of the Achilles tendon

The Achilles tendon is formed by the fusion of fibres from the medial and lateral bellies of the gastrocnemius and the soleus The partial rupture of the tendon can involve a greater or smaller section of

1) the medial portion of the tendon
2) the lateral portion of the tendon
3) *the central or the soleus portion of the tendon*
4) all three portions of the tendon as in some central ruptures but most of the tendon fibres remaining intact

Histologically the partial rupture is characterized by devitalized tendon tissue with frayed fibrous structure and around these areas granulation tissue which, according to the age of the rupture is transformed into more or less tendon like connective tissue

History

Complete subcutaneous rupture of the Achilles tendon was first described by Paré in 1575 and has since been described by several authors for instance Petit in 1724 af Acrel in 1759 and Arner & Lindholm in 1959 The last named authors presented a study of 92 patients operated on for subcutaneous Achilles tendon rupture which was complete in all the cases They hold that isolated partial rupture of the free portion of the Achilles tendon does not occur or is at least extremely rare

Arner & Lindholm (1959) state that of all the published cases of so called partial rupture which were explored operatively only one (Kolb & Salem 1953) could from the functional standpoint possibly be regarded as partial On the basis of his observations in a series of 240 cases from the Bohler Clinic in Vienna all being cases of complete Achilles tendon rupture Schonbauer (1955 1966) questions the existence of the partial rupture

Kolb & Salem (1953) report 2 cases of Achilles tendon rupture treated by operation in one case the rupture involved half the tendon The rupture may possibly be judged as partial in the other case as well According to Kolb & Salem the reason why only a small number of partial ruptures have been described would be that because of the clinical methods of examination a difference between "strain — Zerrung — and partial rupture of the tendon cannot be definitely established They also state that it is difficult to diagnose a partial rupture clinically Ignorance of this injury however can lead to deterioration or complete rupture as a result of unsuitable treatment (forced exercise massage)

Wedel (1954) and van de Kamp (1954) each described a case of partial Achilles tendon rupture In Wedel s case there was a medial intact tendon remnant the thickness of a wool thread *2 mm in thickness* Schonbauer (1955) believes that both cases were misinterpreted and that in both of them the intact portion of the tendon consisted of the *plantaris* tendon which according to Alker (1957) can descend medial as well as in front of behind and lateral to the Achilles tendon

In 1960 Solheim reported a series of 76 cases of complete and 1 case of partial rupture the latter was initially treated conservatively for 5 months

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Present series

The series comprises 24 patients who over the 4 year period 1964—1967 were examined for Achilles tendon injuries at the Department of Surgery and the Physiotherapy Department at Serafimerlasarettet in Stockholm (Tables I—III) and who had undergone operation for the injury at least 1 year previously (see below) * It will be seen from Tables II and III that all the patients excluding one (no 3) engaged in some form of sport The explanation of this is that the author is physician to the Swedish Amateur Athletic Association and to football and ice hockey teams of top class players In this capacity I came into direct contact with 13 patients The other 11 were referred to me because of my interest in sports injuries 6 patients were referred from hospital physicians or private practitioners in the Stockholm area and 5 from hospital physicians outside the Stockholm area Nine cases were by the referring physician diagnosed as achillotendinitis and 2 as rupture of the gastrocnemius muscle

The distribution by sex and age is shown in Table I It will be seen that there is only one woman (case 9) The patients can be divided into a lower age group of 19—29 years including champion athletes alone (Table II)

TABLE I

Age and sex distribution

Age (years)	Men	Women	Total
19	1	0	1
20—29	10	0	10
30—39	1	0	1
40—49	8	0	8
50—59	1	1	
60—65		0	2
Total	3	1	24

* I have operated upon a further 15 patients but as the observation period in these cases less than 1 year they are not included here

without any effect Operation revealed a rupture of half the tendon with calcium deposits In 1964 Lanz described a case of partial spontaneous transverse rupture of the Achilles tendon, 2 cm above the insertion in a 62-year old woman He also discussed the question whether or not the Achilles tendon always ruptures completely In Lanz's opinion the diagnoses in the published cases of partial rupture treated conservatively can not be regarded as confident and he considers that the sporadic cases treated operatively and published as partial ruptures must be viewed very critically According to Baetzner (1957), individual bundles of tendon fibres can rupture at different levels and thus simulate partial ruptures Lanz considers that exposure of the whole tendon is necessary in order to *prove that a true partial rupture has occurred*

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TABLE III
*Athletes**

Case no	Age yr	Occupation and branch of sport	Causal violence	Interval between rupture and operation
3	46	Electrician	a) Blow of reinforcing iron bar b) Stumbled on a wooden board	18 months (partial) 2 days (complete)
5	4›	Engineer skier	S idden push off in the cold	12 months
7	51	Carpenter footballer	Joggling after training	12 months
8	40	Electrical fitter orienteerer skier	Cycling uphill	14 months
9	54♀	Eng neer cross country runner gymnast	Slipped during cross country running in the mountains	6 weeks
10	‹5	Colonel walking	Sl pped on kerb	weeks
11	54	District manager allround ori nteerer	Tr pped o er on kerb	7 weeks
1	4	Manager cycl st skier	Caught foot butted on calf by ram	5 months
13	38	Eng neer handball player	Handball match	10 weeks
16	63	Foreman athlete	a) Physical exercises b) Jumped to dodge traffic on crossing street	7 weeks 4 weeks
1	47	Eng neer allround sportsman o ienteerer skier	a) 1500-metre run b) Sk ng	10 years? 2 months
0	43	Bank clerk orienteerer	C oss country race	9 months
1	45	Taxi dri er track and field thlete	a) Road race b) Football c) 400 metre run	7 months ? months 1 day

TABLE II

Champion athletes

Case no	Age yr	Occupation and branch of sport	Causal violence	Interval between rupture and operation
1	24	Engineer medium distance runner	Spurt in a 3000 metre race	6 months
2	25	Policeman skier	Excessive weight bearing on foot in grappling with a drunkard	1 month
4	29	Engineer ice hockey player	Pulled up suddenly at ice hockey	7 weeks
6	29	Electrician footballer	Tripped over at work	8 months
14	24	*University student long* distance runner	*Barefoot running*	*6 months*
15	22	*Buyer hurdler*	*Slipping*	*4 months*
18	27	Farmer long distance *runner*	Spurt in a 10 000 metre *race*	5 day
19	8	Engineer cross country runner	Tripped over tree root	12 months
22	22	Student of technology sprinter	Violent push off at a 100 metre race	3 months
23	23	Gymnastics master medium distance runner	Training pressure of shoe stiffener	(months
21	19	Office clerk medium distance runner	800 metre race on wooden floor	8 months

and a higher age group of 38—65 years comprising various kinds of athletes (Table III) The latter group includes the only patient who was not an athlete (case 3) but who was physically very active

The following intervals had elapsed between operation and examination

1 year — 11 cases
2 years — 10 cases
3 years — 3 cases

* In the following the term athlete will refer to a person who performs strenuous physical exercise 2—3 times a week

Aetiology

Subcutaneous rupture of the Achilles tendon has been attributed to pathological processes in the tendon tissue and/or trauma. Rupture of a pathologically changed tendon can result from insult which is so slight that the patient himself does not notice it, so called spontaneous rupture (Christensen 1954). Several authors from Friaques (1891) to Boyd (1945) have described numerous factors that lower the strength of the tendon such as syphilis, gonorrhoea, tuberculosis, uratic arthritis and pyogenic infections. Other causes are tendinitis suggested by Malbec (1935) and Silfverskiold (1941) and tumours and cysts by Christensen. Repeated minor traumata particularly in certain occupations would also lead to rupture of the small vessels with accompanying impaired circulation which could predispose to later ruptures (Albrecht 1925, Bate 1951, Wachs 1951, Borsay 1952). Oral steroid treatment (Lee 1961, Gjone 1962, Melmed 1965 and others) and local steroid injections in connection with trauma (Lee 1957) have also been discussed as aetiological factor.

Of the above listed causal factors steroid injections and trauma played a part in the present series of cases.

Steroid injections

Since Hollander (1951) published his work on the beneficial anti-inflammatory effect of locally injected hydrocortisone in bursitis and tendinitis this treatment has been widely used in achillo-tendinitis, not least in sports injuries. Wrenn, Goldner & Markee (1954) in an experimental study on dogs report on the effect of cortison on the healing process and the tensile strength of the tendon after severing of the tendon and subsequent suturing. They found that daily intramuscular administration of 10 mg of cortisone per kg body weight for 3 weeks *prevented* excessive formation of peritendinous fibrous tissue but it did not prevent end to end healing of the tendons. On weight bearing exercise it was found that the strength in the sutured area of the tendon was consistently lower than in the control cases. Although the tendon treated with cortisone for 3

2

Occupation and form of athletics will be seen from Tables II and III A striking fact is that heavy manual labour is represented by only 2 cases (farmer and carpenter) as against white-collar and similar occupations by 22 cases

The branches of athletics are mostly of the track-and field type, cross country running, orienteering and skiing, all of which call for greater fitness and require more intense and lengthy running practice with re sulting greater strain on the Achilles tendon Team sports (football, ice hockey, handball) are represented by only 3 cases

In view of the fact that diminished perfusion with impaired oxygen supply to the tendon tissue has been discussed as a causative factor in devitalization of the Achilles tendon (Wuscheck, Kempe & Arent 1966), the haemoglobin values were studied and the following results were ob tained

Hb =	11 9 g per 100 ml	2 cases
	12 7—13 9 g per 100 ml	6 cases
	14 0—15 0 g per 100 ml	15 cases
	16 7 g per 100 ml	1 case

It will be seen that the haemoglobin value was below the lower limit of normal range — 12 0 g per 100 ml — in 2 cases (nos 17 and 18)

TABLE IV

Corticosteroid treatment in partial ruptures of Achilles tendon

Case no	Diagnosis	Before rupture: Number of steroid injections	Before rupture: Interval between injection and rupture	After rupture: Number of steroid injections	After rupture: Interval between rupture and injection
1	Tend nitis	0	—	1	3 months
2	Tendinitis	2	3 months	0	—
3	Tend nitis	0	—	3	6 months
4	Tendinit s	2	2 months	0	—
5	Tendinitis	1	1 year	9	2 weeks
6	Tend nitis	1	1 year	1	3 weeks
7	Tendin tis	0	—	2	1 week
8	Tendinitis	0	—	9	1 week
9	Partial rupture	0	—	0	—
10	Tendin tis	1	4 months	0	—
11	Tendinitis	1	6 weeks	2	11 days
12	Partial rupture	0	—	0	—
13	Partial rupture	0	—	0	—
14	Achillobursitis	0	—	3	2 5 months
15	Tendinitis	0	—	1	3 months
16	Tendinitis	0	—	5	10 day
17	Partial rupture	0	—	0	—
18	Partial rupture	0	—	0	—
19	Tendinit s	1	11 months		
		1	3 months	1	2 weeks
20	Partial rupture	0	—	0	—
21	Tendinitis	2	2 months	0	—
22	Tendin tis	1	5 weeks	0	—
23	Tendinit s	1	3 months	0	—
24	Tendinitis	0	—	1	10 days

a suggestion of dystrophic calcification The appearance of parts of the areas resembled that of thopus

It will be seen from the above account that just over half the patients had not received steroid injections before the rupture In the rest the time-relationships among other factors argue against the possibility that the steroid injections would have been of direct aetiological significance They might have played a part by relieving the patient of the symptoms attending a small rupture or some other injury of the Achilles tendon and so allowed increased weight bearing on the tendon thus being concerned in causing the clinically manifest rupture

weeks, was 40 % weaker than in the controls, the healing in both the cortisone and the control group was adequate for normal tendon function

Asboe-Hansen (1956) and Zachariae (1966), in studies of the local effect of corticosteroids, emphasize that these drugs inhibit new formation of connective tissue and produce an anti inflammatory effect, but may cause increased degeneration and necrosis of the tissues

Only in 3—4 of the published cases of partial subcutaneous rupture of the Achilles tendon can the diagnosis probably be regarded as confident As my material from the Department of Surgery at Serafimerlasarettet over the period 1964—1966 includes 24 cases of partial rupture the question arises whether these could be complications of local steroid treatment of achillotendinitis, this treatment being relatively widely used during this period of time The series has therefore been analysed with respect to the number of local steroid injections before and after the occurrence of suspected rupture and the interval of time between injection and rupture (Table IV)

It will be seen from Table IV that intra- or peritendinous cortico steroid injection had been given

Before rupture	6 cases
Before and after rupture	4 „
After rupture	8 „
Neither before nor after rupture	6 ,

Accordingly, 14 patients had not received any steroid injection before the rupture Out of the 10 patients who had been given local steroid injection before the rupture 2 (nos 5 and 6) had received one injection about 1 year before the rupture and had had no trouble from the Achilles tendon during this period of time, in spite of intense activity It is therefore hard to believe that the injection in these cases could have been of any aetiological significance In Cases 2, 4, 10, 19 21 and 23 the injection which caused relief of symptoms was given 2—4 months before the partial rupture In at least 4 of these cases the local symptoms present at the time of the injection were in a part of the tendon other than the site of rupture Patients nos 11 and 23 received one steroid injection 5 and 6 weeks, respectively before the injury and were free from symptoms until they sustained the rupture

Histological examination of the surgical cases showed no difference in the picture between the steroid treated and the non steroid treated patients with the possible exception of Case 22 in which the devitalized tendon tissue was found to contain a few small defined necrotic areas with

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2	Tendinitis	2	3 months	0	—
3	Tendinitis	0	—	3	6 months
4	Tendinitis	2	2 months	0	—
5	Tendinitis	1	1 year	9	2 weeks
6	Tendinitis	1	1 year	1	3 weeks
7	Tendinitis	0	—	2	1 week
8	Tendinitis	0	—	9	1 week
9	Partial rupture	0	—	0	—
10	Tendinitis	1	4 months	0	—
11	Tendinitis	1	6 weeks	2	11 days
12	Partial rupture	0	—	0	—
13	Partial rupture	0	—	0	—
14	Achillobursitis	0	—	3	2 5 months
15	Tendinitis	0	—	1	3 months
16	Tendinitis	0	—	5	10 day
17	Partial rupture	0	—	0	—
18	Partial rupture	0	—	0	—
19	Tendinitis	1	11 months	0	—
		1	3 months	1	2 weeks
20	Partial rupture	0	—	0	—
21	Tendinitis	2	2 months	0	—
22	Tendinitis	1	5 weeks	0	—
23	Tendinitis	1	3 months	0	—
24	Tendinitis	0	—	1	10 days

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It will be seen from the above account that just over half the patients had not received steroid injections before the rupture In the rest the time-relationships among other factors argue against the possibility that the steroid injections would have been of direct aetiological significance They might have played a part by relieving the patient of the symptoms attending a small rupture or some other injury of the Achilles tendon and so allowed increased weight bearing on the tendon thus being concerned in causing the clinically manifest rupture

Trauma

The Achilles tendon can be ruptured by direct or indirect violence. It is believed that rupture can occur when the violence is applied at right angles to a tense tendon (Kolb & Salem). Indirect violence is considered to be the more common cause. Arner & Lindholm, in analysing the causes of complete rupture, distinguished between three main types of indirect violence:

1) Pushing off with the weight-bearing forefoot flexed in a plantar direction while extending the knee joint, for instance at the start of a sprint, in running and in some types of jumps. In this coordinated movement the calf muscle is maximally contracted;

2) Sudden and unexpected violent dorsiflexion of the ankle when the foot is in an intermediate position, for instance in slipping on a stair or stumbling into a hole, the patient falls forward and the heel sinks down suddenly. In this type of violence the calf muscle is usually moderately contracted and becomes maximally contracted in the sudden reflected and uncontrolled movement.

3) Violent dorsiflexion of the foot flexed in a plantar direction, for instance on jumping or falling from a height. The calf muscle is strongly contracted and the sudden violence to the foot leads to marked stretching of muscle and tendon.

The Achilles tendon, being one of the strongest tendons of the body, takes a load of about 240 kg at ordinary walking and of about 600 kg at running. The load may amount to 900 kg at very swift running (Carlsoo 1968). Arner, Lindholm & Orell (1959) in their series of 74 cases of complete rupture examined histologically noted degenerative changes in the tendon in all the cases, even in those of the patients operated on only a few hours after the injury (see also Davidsson 1956). They attributed the histological changes to impaired blood supply. Angiographic and microangiographic studies by Lagergren & Lindholm (1959) have shown that the most frequent site of rupture of the Achilles tendon is the segment least vascularized, namely 2—3 cm above the insertion of the tendon. Arner & Lindholm give the following explanation of the Achilles tendon rupture. Training and increased activity of a muscle lead to hypertrophy and increased vascularisation of muscular tissue (Petrén, Sjostrand & Sylven 1936), and probably also of tendon tissue during an athlete's active years. If these are followed by inactivity, degenerative changes will occur in the tendon tissue with resulting impaired tensile strength. Ricklin (1962) states that the elasticity diminishes rapidly after age 30 with progressing

obliteration of the vessels of the tendon Degeneration and fragmentation of the tendon fibres will reduce the tensile strength of the tendon

Ricklin also maintains that in highly active athletes exhaustion is a factor that plays an important part in causing structural changes in the Achilles tendon with resulting greater tendency to rupture A comparison is in vitably made with the insufficiency fractures of the fibula which are largely on the same level as the Achilles tendon ruptures and which occur relatively often in champion athletes during periods of hard training As regards the aetiology of these fractures they have been attributed for instance to a change in the submicroscopical bone crystals and dissolution of the tissue connecting them (Henschen 1936)

On the ba is of Cummins (1949) observation that the tendon fibres from the gastrocnemius and the soleus converge as the descend while rotating toward the insertion on the calcaneus Christensen (1954) suggested that in running and jumping there occurs a saw like friction between the tendon fibres especially in persons in whom there is not satisfactory coordination between the three muscle tendon portions This would explain why the tendon often ruptures in untrained athletes

Present series

The s ries of cases of partial rupture of the Achilles tendon numbering altogether 24 can be divided into two groups one comprising 11 active champion athletes between 19 and 29 years old who were training almost daily all the year round The other group consisted of 13 athletes including one woman whose ages ranged from 38 to 65 years The majority of the latter group had never given up sports completely Several of them were still very active taking part in for instance orienteering races and the Vasa Ski Race (skiing competition over a distance of 85 km)

The first group cannot be regarded as representative of *Arner & Lindholm*s th one as all of them were in their most active period of athletics Four were or had recently been members of the *Swedish* international athletic team the youngest one 19 years old being a member of the junior team and considered to be *one of our* most promising medium distance runners The others were champion ice hockey players footballers and track and field athletes — medium distance and *long distance* running The mean age was 25 (24 8) years It was of course difficult to establish the exact time that had *elapsed* between the injury and the operation at which specimens for histological examination were taken a some of the patients reported s veral *injuries* In one case however the exact interval of 5 days could be established After careful history *taking* and analyses

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3) Violent dorsiflexion of the foot flexed in a plantar direction for instance on jumping or falling from a height The calf muscle is strongly contracted and the sudden violence to the foot leads to marked stretching of muscle and tendon

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The histological changes in subcutaneous complete rupture of the Achilles tendon have been described earlier by for instance Kolb & Salem in 1953 (6 cases) Davidsson in 1956 (5 cases) Orell in 1958 (14 cases) and Arner Lindholm & Orell in 1959 (74 cases) The last named authors found characteristic degenerative and necrobiotic changes in the tendon tissue in all their cases (see page 20)

Own investigations*

The histological findings are recorded in Table V The *champion* group (Table II) includes one patient (no 18) with a partial rupture that was examined only 5 days after the injury Gross examination showed relatively extensive haemorrhage along the rupture ends The histological picture of the resected rupture ends was that of devitalized tendon tissue with altered collagen stainability and non stainable endoplasm areas Minimal inflammatory cell infiltration was seen in a few places around the vessels as well as slight fibrin exudation There were virtually no formation of granulation tissue and no signs of newly formed tendon like granulation tissue

In the rest of the patients in the champion group — irrespective of the time interval between injury and operation — the histological examination of the resected rupture ends showed partially devitalized tendon tissue with obliterated fibrin structure and in places fraying of the collagen bundles altered stainability and decolourized poorly stainable or non-stainable endoplasm areas To the devitalized tendon tissue were attached fine or coarse streaks of loose granulation tissue rich in collagen and of a thin wavy structure that deviated from the collagen structure of normal tendon tissue The tendon like granulation tissue in cases 6 and 19 in which the time interval between injury and operation was 12 months and 8 months respectively was highly vascularized and inflammatory infiltrates were seen around the vessels in some places there were also

* The histological examinations were carried out in cooperation with Hans Nordenstam, prosector at the Department of Pathology Serafimerlasarettet

of the reported traumata, the approximate time interval could be fairly well ascertained

Some data in the most active group are set out in Table II Table III shows data from the athlete group, but it should be noted here that most of these patients had, in fact, never given up sports entirely

In those cases in which a long time had elapsed between the injury and the author's first examination of the patients, it was difficult to establish the nature of the trauma With due reservations, the distribution of the causal violence, according to the Arner-Lindholm scheme (their group 3 not being represented), can be listed as follows

Group 1	*14 cases*
(start of sprint, running)	*(nos* 1, 2, 5, 7, 8, 13, 14, 16, 17, 20, 21, 22, 23)
Group 2	*10 cases*
(slipping)	(nos 3, 4, 6, 9, 10, 11, 12, 15, 18, 19)

The series includes one case in which direct violence was applied to the tendon In the rest of the cases the patients were able to specify one or several similar types of indirect violence as the cause of the rupture

Fig 3 Devitali d tendon tissue partly with complete abs nce of s ainable cell nuclei Fraying of collag n s ructure (Haemotoxylin and eosin x240)

F g 4 H ghly cellular granulation tissue showing foreign body reaction adjoining an old ecr tic area (Haemotoxyl n a d eosin x 40)

Fig 1 Transition from peritendinous fatty tissue to newly formed granulation tissue Areas of chronic cell infiltration (Haemotoxylin and eosin x95)

Fig 2 Transition from devitalized tendon tissue to surrounding sclerosed granulati   tissue Sp rse infl mmatory cell infiltration (Haemotoxylin and eosin x25)

Fig 3 Devitalised tendon tissue partly with complete absence of stainable cell nuclei Fraying of collagen structure (Haemotoxylin and eosin x240)

Fig 4 Highly cellular granulation tissue showing foreign body reaction adjoining an old fracture (Haemotoxylin and eosin x240)

Fig 1 Transition from peritendinous fatty tissue to newly formed granulation tissue Areas of chronic cell infiltration (Haemotoxylin and eosin x95)

Fig 2 Transition from devitalized tendon tissue to surrounding sclerosed granulation tissue Sparse inflammatory cell infiltration (Haemotoxylin and eosin x95)

TABLE V

Gross and histological findings

Case no	Macroscopically	Histologically: Devitalized tendon tissue	Granulation tissue: new	Granulation tissue: old tendon like	Inflammatory cell infiltration: acute	Inflammatory cell infiltration: chronic	Fibrin exudate	
1	xx	xx	x	xx		xx	xx	
2	xx	xx		xx		x		
3	xx	xx		xx		xx	x	N
4	xx	x	x	xx	x	xx	x	
5	(x)	xx		xx		x		
6	xx	xx		xx		x	x	
7	(x)	xx		xx		x		
8	xx	x	x	xx		xx		
9	(x)	xx	x	xx		x		
10	xx	xx	x	xx	x	xx		H
11	xx	xx	xx	xx	x	xx		N
12	xx	xx	x	xx		xx	xx	
13	(xx)	x		xx		xx		
14	(xx)	xx	x	xx	x	xx	xx	H
15	xx	x		xx		x		
16	xx	x		xx		x		
17	xx	x	x	xx	x	xx		N
18	xx	xx	x			x		
19	(xx)	xx	x	xx	x	xx		
20	(x)	xx		xx		x		
21	xx	xx	x	xx	x	xx		H
22	xx	xx	x	xx		x		N
23	x	xx	x	xx		x		
24	x	xx		xx		x		

( ) = Rupture not visible until after incision in tendon
N = Necrosis
H = Haemorrhage

Summary

The histological changes both in the champion group with a mean age of 25 years and in the athlete group with a mean age of 48 years were characterized by devitalized tendon tissue with altered collagen stainability frayed fibrous structure to which attached granulation tissue converted into more or less tendon like connective tissue Newly formed granulation tissue was seen in 14 cases (see Table V) Old tendon like

large areas of loose granulation tissue poor in collagen Lymphomonocytic cell infiltration, mainly perivascularly, was seen in all the cases The degree of inflammation was recorded as minimal to moderate *Some surfaces* were coated with a fibrin-like albumin containing mass (nos 1, 14, 18, 23, and no 12 in the athlete group)

In the two cases with the longest history (nos 6 and 19) histological changes were also seen in the peritenon The excised peritendinous tissue consisted of fatty tissue showing transformation into newly formed granulation tissue, fairly rich in collagen and of a wavy structure Inflammatory changes were seen around the vessels There was no true tendon sheath structure No synovial membrane was visible The picture resembled mainly that of peritenon with fatty tissue and newly formed granulation tissue of tendon like appearance

The histological findings in the *athlete group* (Table III) were largely consistent with those in the champion group, in that ' the collagen fibres were in places interrupted by granulation tissue, which indicates that partial rupture must be present (case 9)

In 4 cases (nos 3, 11, 17, and no 22 in the champion group) defined areas of necrosis were found in the devitalized tendon tissue Suggested dystrophic calcification was noted in the necrotic areas Parts of the areas were almost tophus-like in appearance (nos 17 and 22)

In patient no 17, who had a possibly 10-year old rupture a history of achillobursitis, and recurrent symptoms of trouble with the tendon 2 months before operation, histological examination showed not only the *usual partial devitalization of tendon tissue but also profuse old and new* formation of granulation tissue Here and there mainly in this granulation tissue, the collagen showed changes most closely resembling myxomatous degeneration Foreign-body reaction was seen in these areas This patient had not received any form of steroid therapy, nor any other specific treatment

In view of the fact that several of the patients had earlier received local steroid injections and that in a few cases operation revealed a few yellowish white deposits in the peritenon the specimens were also examined for the presence of foreign body granulomas or deposits of foreign matter but no such lesions were found in any of the cases Analysis of the observed deposits at hormone and chemical laboratories did not show any steroid substance

Inflammatory monolymphocytic cell infiltration perivascularly was seen *in all the cases of this group* minimal in the fresh ruptures and more profuse in the older ones Ingrowth of vessels was occasionally seen in the devitalized tendon remnant

Considering the pathology (see the foregoing) the patient would be exp cted to suffer tenderness over the rupture site and pain on weight bearing It will be seen from Table VI that swelling tenderness and pain on weight bearing were in fact present in virtually every case These symptoms occur however in several pathological conditions involving this region The almost invariably experienced stabbing or pricking pain on suddenly increased activity and weight bearing is more specific to the partial rupture The pain is probably associated with stretching of the injured tissue

Some patients complained of stiffness of the tendon in the morning and after they had been sitting still for a long time and also of occasional aching at rest The stiffness was most marked in cases of fresh rupture and was then probably attributable to oedema and swelling of the ruptured area in cases of older rupture there was also profuse formation of granulation tissue and adhesions to the peritenon

In 17 of the present cases the patients complained of weakness of the calf and difficulties in rising on the toes or in controlling the foot when attempting to run The feeling of weakness can be associated with the loss of function of parts of the muscle tendon unit and varies with the extent of the rupture The limiting effect of pain could also be a contributing factor

The cause of the condition as stated by the patient was trauma for instance slipping or the like during athletic exercise (11 cases) Some of the patients regarded the injury as insignificant and not worth mentioning at the time some had even forgoten all about it by the time they appeared for the first examination But after careful questioning it was usually possible to discover some insult in the form of excessive weight bearing In most cases this had been accompanied by the afore mentioned shooting stabbing pricking or jarring pain or a sensation of being struck with a whip (23 cases) Some patients described the pain as intense but to many it appeared slight and at first of no importanc

In 8 cases the patients reported a sensation of snapp ng or tearing of the Achilles tendon Such an experience is in fact consistent with the

granulation tissue was found in all the cases, except no 18 with a partial rupture of only 5 days' standing In all the cases there was minimal to relatively profuse perivascular lymphomonocytic cell infiltration as evidence of post-traumatic inflammation

Acute inflammatory cell infiltration was seen in 7 cases (nos 4, 10 11, 14 17, 19, and 20) and chronic cell infiltration in all the 24 cases

As regards the time for the histological changes to develop from the acute to the chronic stage, the limit can probably be fixed at about 7 days After this time it was not possible to determine the age of the rupture Chronic changes were the predominating histological findings throughout the series

No vascular changes were demonstrated in the present cases

In those cases in which the rupture ends are not distinctly visible macroscopically the histological changes associated with a partial rupture of the Achilles tendon may be defined as follows Devitalization of the tendon tissue, in which the collagen fibres in places have been replaced by granulation tissue

Diagnosis

As was mentioned earlier many authors doubt the existence of partial rupture of the Achilles tendon Kolb & Salem state, however that tiredness and insignificant pain are often the only symptoms of partial rupture and that therefore the diagnosis is sometimes very difficult if not impossible

In the present series of cases the diagnosis was based on

1) the case-history
2) clinical examination
3) X ray examination
4) electrophysiological examinations

The case-history

Data relating to the patient s physical activity are of importance to the diagnosis as are information concerning lengthy periods of hard training on surfaces that lead to greater demands being placed on the Achilles tendon such as hard icy roads wooden floors etc Newly added items on the training programme and any injuries are analysed

The subjective symptoms have been described in the foregoing (Page 29) and are shown in Table VI The stabbing jarring or pricking pain in the Achilles tendon and the feeling of a tear or an audible snap in the region of the tendon give rise to strong suspicion of partial rupture of the Achilles tendon

Clinical examination

The findings by clinical examination are set out in Table VII *On inspection* of the tendon region with the patient standing erect turning his back to the examiner and with equal weight *bearing on both feet* the injured tendon appeared locally or to the whole of its extent *increased in width* in 23 cases *Ecchymoses on the back* of the heel extending below both malleoli were seen in the three cases in which the rupture had occurred 1—5 days before the examination When the patient was standing

TABLE VI

Subjective symptoms

Case no	Tenderness	Stiffness	Feeling of weakness	Pain on weight bearing	Sharp pain	Feeling of tear
1	x	x	x	x	x	x
2	x		x	x	x	x
3	x		x	x	x	
4	x	x	x	x	x	x
5	x	x		x	x	
6	x	x	x	x	x	
7	x		x	x	x	
8	x		x	x	x	
9	x		x	x	x	
10	x	x	x	x	x	x
11	x		x	x	x	
12	x		x	x	x	x
13	x		x	x	x	
14	x	x	x	x	x	
15	x			x	x	x
16	x	x	x	x	x	x
17	x	x	x	x	x	
18	x	x		x	x	x
19	x	x		x	x	
20	x	x		x		
21	x		x	x	x	x
22			x	x	x	
23	x			x	x	
24	x			x	x	
Total	23	11	17	24	23	8

true course of events When distinct it should give rise to strong suspicion of rupture

In most cases the tendon injury did not interfere with the patient's work Only patient no 3, an electrician suffered limitation of movement in his work, especially on climbing ladders because of reduced muscular strength in the plantar flexors of the foot

The objective symptoms are listed in Table VII As in most cases they were not demonstrated before careful clinical examination they *will* be described under that heading (see the following)

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1	x	x	x	x	x	x
2	x		x	x	x	x
3	x		x	x	x	
4	x	x	x	x	x	x
5	x	x		x	x	
6	x	x	x	x	x	
7	x		x	x	x	
8	x		x	x	x	
9	x		x	x	x	
10	x	x	x	x	x	x
11	x		x	x	x	
12	x		x	x	x	x
13	x		x	x	x	
14	x	x	x	x	x	
15	x			x	x	x
16	x	x	x	x	x	x
17	x	x	x	x	x	
18	x	x		x	x	x
19	x	x		x	x	
20	x	x		x		
21	x		x	x	x	x
22			x	x	x	
23	x			x	x	
24	x			x	x	
Total	23	11	17	24	23	8

true course of events When distinct, it should give rise to strong suspicion of rupture

In most cases the tendon injury did not interfere with the patient s work Only patient no 3 an electrician suffered limitation of movement in his work, especially on climbing ladders because of reduced muscular strength in the plantar flexors of the foot

The objective symptoms are listed in Table VII As in most cases they were not demonstrated before careful clinical examination they will be described under that heading (see the following)

TABLE VII

Objective symptoms

Case no	Increase in diameter of tendon plus tenderness on palpation	Defect in tendon contour	Induration of tendon	Muscle atrophy	Reduced muscle tone	Increased dorsal extension	Fluctuation
1	x	x	x	x	x		
	x	x	x	x	x		
3	—		x	x	x	x	
4	x	x	x			(x)	
5	x		x	x	x	x	
6	x	x	x				
7	x		x	x	x	(x)	x
8	xx		x			x	
9	x		x				
10	x	x	x			x	
11	x		x	x	x	(x)	x
12	x	x	x	x	x	x	
13	xx	x	x			x	
14	x		x	x	x		
15	x		x	x	x	x	
16	x	x	x	x	x	x	
17	xx	x	x				x
18	x		x				
19	x		x	x	x		
20	x		x	x	x	(x)	
1	x	x	x				
2	x	x	x	x	x	(x)	
3	x		x				
4	x		x	x	x		
Total	23	11	24	14	14	8+(5)	3

( ) = < 5

of the respective belly Thompson's (1960) test performed with the patient standing on all fours elicited normal plantar flexion in all the cases though with slightly reduced *muscular strength* in 2 cases when resistance was applied by the examiner's other hand Increased *dorsal extension in the talocrural joint* as a sign of lengthening of the muscle and tendon was noted in several cases Greatly increased dorsal extension (to 5—15° more



Fig 5 Partial rupture of gastrocnemius component of left Achilles tendon In the right uninjured leg the contracted gastrocnemius muscle bellies are distinctly seen muscle tone normal on palpation The injured leg shows no typical contraction of the gastrocnemius muscle bellies palpable reduced muscle tone

on tiptoe with equal weight bearing on both forefeet more or less distinct *muscle atrophy* was seen in 14 cases *in 3 involving the medial and in 6* the lateral gastrocnemius belly and in 5 being generalized atrophy of the triceps surae The circumference of the calf was 1 5—2 cm less than that of the healthy leg In all the cases in which distinct muscle atrophy was noted at the examination palpation was believed to reveal reduced *muscle tone*

TABLE VII

Objective symptoms

Case no	Increase in dia meter of tendon plus tenderness on palpa t on	Defect in tendon contour	Induration of tendon	Muscle atrophy	Reduced muscle tone	Increased dorsal extension	Fluctua tion
1	x	x	x	x	x		
	x	x	x	x	x		
3	—		x	x	x	x	
4	x	x	x			(x)	
5	x		x	x	x	x	
6	x	x	x				
7	x		x	x	x	(x)	x
8	xx		x			x	
9	x		x				
10	x	x	x			x	
11	x		x	x	x	(x)	x
1	x	x	x	x	x	x	
13	xx	x	x			x	
14	x		x	x	x		
15	x		x	x	x	x	
16	x	x	x	x	x	x	
1	xx	x	x				x
18	x		x				
19	x		x	x	x		
20	x		x	x	x	(x)	
1	x	x	x				
2	x	x	x	x	x	(x)	
3	x		x				
4	x		x	x	x		
Tot 1	3	11	24	14	14	8+(5)	3

( ) = < 5

of the respective belly Thompson s (1960) test performed with the patient standing on all fours elicited normal plantar flexion in all the cases though with slightly reduced *muscular strength* in 2 cases when resistance was applied by the examiner s other hand Increased *dorsal extension in the talocrural joint* as a sign of lengthening of the muscle and tendon was noted in several cases Greatly increased dorsal extension (to 5—15° more

3

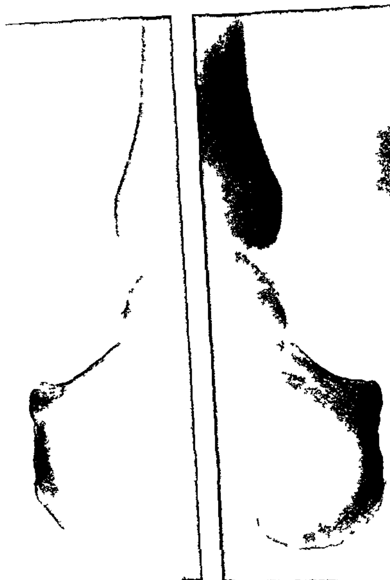
than normal) was present in 8 cases It was noted in patients with ruptures that involved a relatively large section of the tendon and were of relatively long standing An increase of dorsal extension to a few degrees more than normal was seen in 5 patients, but such an increase would be within the limits of normal differences in the range of movement between the right and the left ankle joint With the weight-bearing at walking etc, after a relatively deep-going partial rupture the thin remaining part of the tendon and its muscle portion will be gradually and increasingly stretched and permanently lengthened, which would explain the increase of dorsal extension

Palpation of the Achilles tendon was done with the patient supine, the foot flexed in a plantar direction and the knee flexed, and with the patient lying prone or standing on his knees, the foot in mid-position and standing on his toes The tendon could thus be palpated right through relaxed, moderately tense, and maximally tense A *fusiform thickening* of the Achilles tendon was noted in 23 cases, over an area 2—6 cm (18 cases) and 6—10 cm (6 cases) above its insertion, and corresponding to the rupture site The thickening involved the whole tendon in 4 cases, in some mainly the medial, the dorsal, or the lateral portion, with marked tenderness on palpation, in 3 cases there was distinct fluctuation In all the patients (24 cases) palpation of the ruptured tendon revealed an indurated section that was firmer that the normally relatively soft elastic consistence of uninjured tissue Suspected *dents or small defects* in the tendon contour were also palpated in 9 cases and some *irregularity* in the contour or the peritenon in 2 cases

X-ray diagnosis

The Achilles tendon is surrounded by loose tissue mostly fatty tissue and can therefore be seen in a radiograph The radiographic appearance of the Kager triangle , described by Kager (1939) has been regarded as diagnostic of subcutaneous complete rupture of the Achilles tendon Arner Lindholm & Lindvall (1959) state that deformation of this triangle which in lateral views is bounded by the Achilles tendon the calcaneus and the deep flexor tendons is pathognomonic for complete subcutaneous Achilles tendon rupture, when the tendon contour curves away dorsally from the posterior surface of the calcaneus between the insertion of the tendon and the upper margin of the corner of calcaneus and then proximal to this point deviates ventrally

After subcutaneous partial rupture of the Achilles tendon a change in "Kager s triangle also occurs in some cases (see below at 3) By infiltra



F g 6 X ray f ndings in Case 19
Right Normal Achilles tendon of contralateral side w th Kager s triangle displayed as a triangular l ght p rt the base formed by the upper margin of the calcaneus and the s de by the entral contour of Achilles tendon and the dorsal contours of the deep flexor tendo s
Left Achilles tend n partially ruptured centrally Kag r s triangle reduced and deformed by tend n thic en g and soft tiss e infiltration and the tendon contour irregularly out l ned aga nst the fatty spa e Small a eas of calcification are also seen in the soft tissue space

TABLE VIII
X-ray findings

Case no	Thickening of tendon	Tendon indistinctly outlined	Infiltration	Calcification
1	x			
2	x			x
4	x			
6	x			
8	x	x	x	
10	x			
11	x			
12	x	x	x	
13	x	x	x	
14	x		x	
15	x	x	x	
16		x	x	
17	x		x	
19	x	x	x	x
20	x			
21	x	x	x	
22		x	x	
23		x		
24	x	x	x	
Total	16	10	11	2

In 3 patients with injuries of both Achilles tendons simultaneous X ray of contralateral tendon showed local thickening but no other abnormalities

tion into the fatty space it becomes more or less symmetrically narrowed or reduced in comparison with that on the contralateral uninjured side

X-ray examination was performed in 19 cases The observed changes are recorded in Table VIII

The following changes were seen

1) Local more or less extensive, thickening of the tendon (16 cases)
2) Tendon contour less distinct than normal and irregularly outlined against the fatty tissue (10 cases)
3) Soft-tissue space infiltrated (11 cases), in some cases round the whole tendon, in others dorsally or only ventrally

These findings proved to be of value in locating the rupture site especially when the first superficial inspection of the exposed tendon at operation did not show any obvious change Exposure of the section of the tendon corresponding to the part showing radiographic changes revealed a

partial rupture situated ventrally in the cross section of the tendon (case 24)

Soft tissue X ray showed in 2 cases (nos 2 and 19) minor areas of calcification ventral to the Achilles tendon which were interpreted as calcification of haematomata after rupture In one of these cases (no 19) in which the tendon appeared intact on inspection incision of the tendon revealed a central rupture with calcium incrustation both in the proximal and in the distal rupture ends

The contour could not be seen in 1 case (no 14) and therefore the rupture could no be assessed radiographically

Soft tissue X ray is an important part of the examination in cases of suspected partial rupture of the Achilles tendon In some cases in which neither the clinical nor the electromyographic examination yielded any conclusive evidence of partial rupture the X ray findings provided a valuable basis for the decision whether or not to operate

Electrophysiological examinations*

So far as is known electrophysiological studies of partial tendon ruptures in man have not been described earlier A preliminary report of the studies in the present cases has been published (Persson 1967) and a more detailed account will be published elsewhere (Persson & Ljungqvist in the press)

The studies comprised

1 *Electromyographic recording*

of voluntary activity using concentric needle electrodes in the triceps surae Cases 2—24 were examined by this method The amount of such activity was compared between corresponding electrode positions in the healthy and the affected leg and between the lateral and medial gastrocnemius bellies and the soleus muscle of the same leg To activate the muscle under examination the patient was told to stand on his toes bearing the weight of the whole body on the leg to be examined

In cases of partial rupture the amount of motor unit activity was found to be reduced in the muscle portion whose tendon had been torn The pattern of activity was also changed Most of the action potentials recorded were of small or medium amplitude whereas the large potentials which always appear at moderate to strong contraction were lacking (see Fig 7 A)

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* Performed in cooperation with Ass Prof Anders Persson Department of Clinical Neurophysiology Karolinska Sjukhuset

TABLE VIII
X-ray findings

Case no	Thickening of tendon	Tendon indistinctly outlined	Infiltration	Calcification
1	x			
2	x			x
4	x			
6	x			
8	x	x	x	
10	x			
11	x			
12	x	x	x	
13	x	x	x	
14	x		x	
15	x	x	x	
16		x	x	
17	x		x	
19	x	x	x	x
20	x			
21	x	x	x	
22		x	x	
23		x		
24	x	x	x	
Total	16	10	11	2

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tion into the fatty space it becomes more or less symmetrically narrowed or reduced in comparison with that on the contralateral uninjured side

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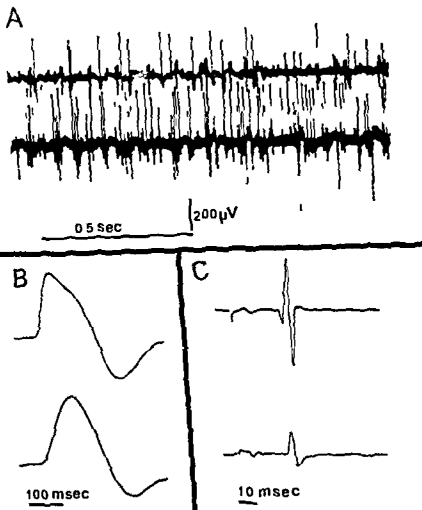


Fig 7

CASE 24 E M G recordings in a patient w th partial rupture of the tendons of the lateral gastrocnem us and soleus muscles

A E M G from lateral (upper traci g) and medial (lower tracing) gastrocnemius belly

B Contraction curve and C H reflex from the affected (upper tracings) and the healthy leg
N t shortened contraction time due to *rupture of the soleus* tendon and deformed contraction curve due to gastrocnemius rupture

Organic lesion of the peripheral or central nervous systems was not present in these cases Yet, as was evident from the electromyograms the patients were unable to perform maximal activation of the muscles A similar functional disturbance has been shown by Blom & Hagbarth (1966) in muscles of amputation stumps, where the tendons or muscles had been divided In their cases as well as in ours there was probably a changed proprioceptive inflow from the muscles, which led to a disturbance of the feed back mechanisms This would be the primary cause of the functional paresis Pain played no significant part in these cases, none of the patients reported pain from the tendon region on activation of the muscle during the examination Moreover, inhibition by pain could hardly have produced the observed asymmetry of the electrical activity

2 *Analysis of the "H-reflex"*

in the gastrocnemius and soleus muscles This is a proprioceptive muscle reflex mediated via a two-neuron arc (Hoffmann 1922, Magladery et al, 1952), thus being of the same type as the common ankle jerk but, unlike the latter, it is elicited by electrical stimulation of the posterior tibial nerve and not by stimulation of the stretch receptor by tapping the tendon The magnitude of the reflex response may be said to be a measure of the excitability of the motoneuron It was recorded electromyographically with surface electrodes over the various portions of the triceps surae The H reflex was studied preoperatively in cases 10—24

The results showed that a rupture that involves the tendon of the gastrocnemius alone, medially or laterally, has no significant influence on the H-reflex After ruptures of the soleus tendon on the other hand isolated or combined with partial or total rupture of the gastrocnemius there is a significant increase of the H-reflex, the amplitude of the response being 2—3 times larger than in the healthy leg (Fig 7 C) Such abnormally increased reflexes were noted in cases 18 19, and 24 and in 2 cases of total rupture To judge from the results of our studies of total Achilles tendon ruptures, the increase of the reflex does not occur until some time (a few weeks) after the rupture

The phenomenon may seem paradoxical after a tendon rupture the muscle is less stretched than normal and so it would be expected that the muscle spindles should also be lax and that their stimulating influence on the motoneurons of the muscle should be reduced A *decreased* H reflex could therefore have been expected By experiments on animals (Kozak & Westerman 1961) it has been shown however that tenotomy is followed by increased afferent activity from the muscle concerned possibly caused

TABLE IX

Electromyographic and operative findings

Case no.	Preoperative EMG	Findings at operation		
		Medial	Central soleus	Lateral
1	— (Postoperatively lateral)			1 left
	Lateral			1 right
3	Lateral			1 right
4	Lateral	(1)		1 left
5	Lateral		(1)	1 left
6	Pathological probably lateral			1 right
7	Lateral			1 right
8	Uncertain possibly medial	1	(1)	right
9	Uncertain		1	right
10	Lateral			1 left
11	Medial	1		left
12	Lateral — (soleus?)		(1)	1 left
13	Medial	1		(1) left
14	Lateral		(1)	1 left
15	Pathological but difficult to interpret		1	(1) right
16	Medial	1		right
17	Lateral — (medial?)	1		1 left
18	Central — soleus	(1)	1	left
19	Central — soleus		1	right
20	Lateral			1 left
21	Lateral — medial	1		1 left
22	Medial	1		right
23	Medial	1		right
24	Lateral — soleus		1	1 right
Total	Medial 6 (1) Central 3 (1) Lateral 13 Uncertain 3	8+( )	5+(4)	14+(2)

Figures in parentheses = Rupture involved only very small part of fascicle or portion of tendon

operatively verified partial rupture of the *Achilles tendon*. In every one of these 15 cases the extent and localization of the rupture could be correctly predicted on the basis of the results of the electrophysiological examination.

A further 100 patients with long standing symptoms located in the region of the Achilles tendon (*such as pain*, tenderness and swelling of

by a compensatory increase of the activity in the gamma-motoneurons of the muscle, which results in an increase of the monosynaptic response

The observation that in man the reflex is increased after soleus but not after gastrocnemius rupture may be accounted for by the fact that the soleus muscle is of predominatingly slow "tonic type

3 *Analysis of the isotonic contraction curve of the calf muscles*

Muscle twitching was elicited by electric stimulation of the posterior tibial nerve and the plantar flexion of the foot was recorded with a capacitive transducer (Dickinson 1950), which did not interfere with the movement This examination was made in cases 2—24 The contraction time (the time from the foot of the curve to its peak) was measured and the shape of the contraction curve was analysed The contraction time for a mixed muscle is of course determined by its slowest component Accordingly a significantly shortened contraction time was recorded in cases of rupture of the soleus tendon (Fig 7 B) Partial rupture of the gastrocnemius tendon, on the other hand, caused deformation of the contraction curve (Fig 7 B) and prolongation of the contraction time

The results of the preoperative electrophysiological examinations are set out in Table IX, which also shows the rupture site as revealed by operation It will be seen from the table that in 19 out of 23 cases the conclusions drawn on the basis of these examinations with respect to the extent and localization of the partial rupture were in very good agreement with the findings at operation In a further case (no 6) re examination of the film showed that the E M G picture clearly indicated lateral rupture that is, established the correct site Insufficient experience with the method of examination accounts for the uncertainty in the initial interpretation of the findings in this case

In cases 8 and 9, in which the electrophysiological diagnosis was in doubt, the rupture involved the whole or part of the soleus tendon When these patients were examined analysis of the H-reflex had not yet been introduced, nor were any attempts made at using the needle electrode for selective recording from the soleus muscle These factors would explain the failure

The reason why the rupture site in case 15 could not be established in spite of repeated examinations is obscure

All the patients were examined on several occasions postoperatively At check ups 3—6 months after operation E M G was normal in all the cases

The method of electrophysiological diagnosis used in the 23 cases presented in Table IX has since then been applied in a further 15 cases of

TABLE IX

Electromyographic and operative findings

Case no	Preoperative EMG	Findings at operation		
		Medial	*Central* soleus	Lateral
1	— (Postoperatively lateral)			1 left
	Lateral			1 right
3	Lateral			1 right
4	Lateral	(1)		1 left
5	Lateral		(1)	1 left
6	Pathological probably lateral			1 right
7	Lateral			1 right
8	Uncertain possibly medial	1	(1)	right
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10	Lateral			1 left
11	Medial	1		left
12	Lateral — (soleus?)		(1)	1 left
13	Medial	1		(1) left
14	Lateral		(1)	1 left
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16	Medial	1		right
17	Lateral — (medial?)	1		1 left
18	Central — soleus	(1)	1	left
19	Central — soleus		1	right
20	Lateral			1 left
1	Lateral — medial	1		1 left
	Medial	1		right
3	Medial	1		right
4	Lateral — soleus		1	1 right
Total	Medial 6 (1) Central 3 (1) Lateral 13 Uncertain 3	8+( )	5+(4)	14+(2)

Figures in parentheses = Rupture involved only very small part of fascicle or portion of tendon

operatively verified partial rupture of the Achilles tendon In every one of these 15 cases the extent and localization of the rupture could be correctly predicted on the basis of the results of the electrophysiological examination

A further 100 patients with long standing symptoms located in the region of the Achilles tendon (such as pain tenderness and swelling of

varying degree of severity) have been examined No electrophysiological changes of the type found in partial rupture were demonstrated in any of these cases The patients who were not operated upon improved on conservative treatment and the condition was classified as "tendinitis

In another 2 cases E M G showed slight asymmetry of voluntary activity which, in itself, might have been compatible with a small partial rupture The H reflexes and contraction curves were normal At a check up after some weeks E M G was normal in both cases By then, the patients were also symptom-free The question whether these patients had had small partial ruptures cannot be answered Clinical manifestations and other observations argued against this possibility

Differential diagnosis

As will be seen from the description of the symptomatology and diagnosis of the partial Achilles-tendon rupture (see Tables VI and VII), the patient s history and the clinical findings are not pathognomonic The condition can be confused with many other conditions affecting the Achilles tendon and surrounding tissue, such as complete Achilles tendon rupture, tendinitis, peritendinitis, calcaneal bursitis periostitis, and insufficiency fractures These conditions can often be differentiated clinically from a partial tendon rupture by the presence in the latter case of, especially, the jarring pain, feeling of weakness, and muscle atrophy Further, the increased dorsal extension in the ankle joint is absent in all the other conditions except complete rupture In most cases the electrophysiological examinations will help in differentiating with certainty a partial rupture from the above mentioned conditions

In complete rupture of the Achilles tendon the plantar flexion of the foot at Thompson s test is absent This absence is pathognomonic and *therefore, complete rupture need not be confused* with partial rupture

The partial Achilles-tendon rupture can sometimes be difficult to distinguish from *achillotendinitis* whether the latter is in an acute or a chronic stage Antiphlogistic medication has usually a distinct beneficial effect on the tendinitis provided that the Achilles tendon is not subjected to any form of increased activity during the treatment "*Tennis leg* (Arner & Lindholm 1958) — rupture of the medial gastrocnemius aponeurosis and the muscle belly — can often be confusingly like a partial Achilles-tendon rupture, as the pain can primarily be located in the calf and the Achilles tendon both in partial rupture and in "tennis leg But in "tennis leg palpation will reveal transverse distinct local tenderness

and diastasis or induration over the medial gastrocnemius belly E M G may also show some abnormalities in these cases because of limitation of movement by pain but these changes are not characteristic of the injury unlike the E M G findings in partial rupture

Another painful condition affecting the Achilles tendon region and accompanied by symptoms similar to those of partial rupture is *peritendinitis* — involving not only the Achilles tendon but also the tibialis posterior and the peroneal tendons Crepitations occur in peritendinitis The tenderness on palpation is also more extensive and less distinctly localised than in the partial rupture *Bursitis* of the subcutaneous Achilles bursa and of the calcaneal Achilles tendon bursa in particular can cause pain radiating ventrally proximally along the Achilles tendon Bimanual palpation often reveals fluctuation and this can be further verified by aspiration of exudate on puncturing the bursa

A possibility that must not be forgotten is that in athletes *periostitis* of the tibia and fibula as well as the not uncommon *insufficiency fractures of the fibula* can give rise to pain — which is initially difficult to locate — in the back of the lower leg and the Achilles tendon region Palpation and X ray examination of the lower leg and E M G will usually be diagnostic in differentiating these conditions from partial Achilles tendon rupture Ankle sprain with hyperextension strain and injury of the posterior part of the joint capsule should also be considered in the differential diagnosis

Treatment

When an Achilles tendon is torn, the extent of the rupture can vary, from a clinically insignificant tear to complete rupture with complete loss of tendon function Cases of the former type require no treatment, whereas those of the latter result in considerable disability, unless the function of the tendon is restored by surgery The ruptures here designated as partial fall somewhere between these two extremes

In those cases in which the results of investigation argue for the presence of relatively small ruptures the correct procedure would be to try first a period of rest and symptomatic treatment If the patient still complains of distressing trouble or objective symptoms persist at the end of this period, operation should be performed If the symptoms are severe and the rupture is assessed as extensive, the primary treatment should be by operation

Conservative treatment

Because of the way in which it was collected the present series of cases does not include patients with small ruptures and mild transient symptoms Most of the patients (13 cases) had undergone prolonged (6—18 months) conservative therapy consisting of rest short-wave, ultrasonic-wave and X-ray treatment, and had received antiphlogistics (Tanderil® Butazolidin®), local steroid and heparin injections without any noticeable effect Immobilization in plaster for 3—4 weeks had been tried in 3 cases but produced no improvement As soon as the Achilles tendon was allowed weight-bearing beyond ordinary walking symptoms were noted in the form of tenderness, swelling and shooting or stabbing pain

Considering the pathology of the injury (see the following) it may be said that restitutio ad integrum by conservative treatment is impossible There will remain for instance the elongation of the tendon which has been described above The conservatively treated patients in this series also had subjective or objective symptoms of varying degrees of severity which indicated operation

Operative treatment

The aim of the operative treatment was to restore the muscle tendon relation so as to re establish as near as possible its normal function

The operations were carried out under ether anaesthesia (6 cases) extradural anaesthesia (12 cases) spinal anaesthesia (5 cases) or with blocking of the sciatic nerve (1 case) A bloodless field was obtained by compression of the thigh with a pneumatic tourniquet inflated up to a pressure of 550 mm Hg The patient was lying prone on the operation table

The Achilles tendon was exposed with a medial curved incision from the insertion of the calcaneus towards the border between the medial and the lateral gastrocnemius bellies The peritenon was divided in the mid line from the calcaneal insertion After the peritenon had been divided the changed rupture area could be directly observed in 17 cases and also in some cases in which the rupture ends were covered with granulation tissue When the granulation tissue had been removed by blunt dissection or excision the rupture ends were clearly seen No definite pathological changes were seen in 7 cases after the peritenon had been divided The tendon surface looked normal on the whole The guidance provided by E M G and X ray as to the rupture site proved valuable in these cases Careful palpation manually and by means of instruments over the suspected sections revealed softer or firmer parts of the tendon which in some instances showed suggested fusiform thickening A longitudinal incision of the changed part disclosed at a depth of a few millimetres the following types of pathological changes

a) Cavities in which the ends of the ruptured tendon were seen lying retracted from one another and coated with haemorrhages and fibrin deposits (3 cases)

b) Soft granulation tissue without tendon structure (2 cases) further exposure revealed the retracted tendon ends and the diastasis filled with the contour less granulation tissue

c) Induration and adhesions ventrally on the tendon (2 cases) which concealed ruptures situated ventrally and centrally

The appearance of the rupture varied greatly but the following types could be distinguished*

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* The records are taken from the tendon segments mainly affected by the rupture

	Transverse rupture	Oblique longitudinal rupture
Medial gastrocnemius portion	3 cases	3 cases
Lateral gastrocnemius portion	6 cases	8 cases
Central soleus portion	3 cases	1 cases
Total	12 cases	12 cases

After the rupture had been located, granulation tissue and devitalized tendon tissue was excised The continuity of the tendon was then restored by various methods, as seen in Table X End-to end suture was used in 8 cases The operation was especially difficult in those cases in which the rupture was of long standing and the rupture ends were widely separated while at the same time some lengthening of the non-ruptured tendon portion had occurred By longitudinal incision into the border between the ruptured and the intact tendon portion the retracted rupture ends were mobilized to assure as satisfactory apposition as possible In 2 cases in which this could not be done the surgeon divided the intact non ruptured tendon portion and sutured it across the ruptured ends for reinforcement so as to assure adequate apposition In 2 cases the tendon was greatly thickened because of granulation tissue and devitalized tendon tissue centrally After excision the tendon was of normal thickness or slightly thinner than normal In these cases we did no more than apply suture round the cystic cavity with its exposed tendon walls and draw it sufficiently tight for the excised tendon walls to unite closely

In longitudinal oblique ruptures and central ruptures side to side suture was used in 7 cases

Suture and plastic repair with a flap were performed in 5 cases The flap was taken from the common tendon aponeurosis where it appeared most viable Thus, if the rupture was laterally situated the flap was taken from the medial side and swung over laterally to cover the defect With a medially situated defect the procedure was the reverse Loose connective tissue and any hardened tissue dorsally on the flap was removed so that a fresh tendon surface was obtained In order that the tendon contour would be as even as possible, the flap was not unlike Silfverskiold s or Lindholm s technique rotated 180°, as this often results in more or less marked thickening of the tendon contour corresponding to the rotation area The flap was instead turned down without rotation distally with the dorsal freshened up surface over the tendon defect and sutured

TABLE X

Method and result of operation

Method of operation	Number	Excellent	Good
End to end suture	8	8	
Side to side suture	7	7	
Suture plus plastic repair with flap	5	5	
Suture plus plastic repair with plantaris tendon	4	3	1
Total	24	3	1

Suture and plastic repair with the plantaris longus tendon were used in 4 cases in which excision of devitalized tendon and granulation tissue had given a larger longitudinal tendon defect centrally medially or laterally The plantaris longus tendon which in all the cases extended medially was loosened at its insertion on the calcaneus and sutured into the defect When the defect was situated centrally or laterally it was sutured after tunnelling from the medial side into the defect tendon area

All the tendon sutures were made with synthetic suture material (supramid) Peritenon was sutured with catgut which was not used furthest distally however as the tension will be too great at this point when the foot is flexed more or l ss markedly in a plantar direction After skin suture the foot plus lower leg was immobilized in plaster with the foot moderately or in some cases markedly plantar flexed to ensure least possible tension in the suture area

The patients could be discharged from hospital on the 3rd—7th post operative day Before discharge they started to walk about on crutches On discharge they were instructed to carry out toe exercises in the plas er cast and quadriceps exercises Three weeks after discharge the patient was recalled for removal of the plaster and the sutures A new full lower leg plaster cast was applied the plantar flexion of the foot being reduced as much as possible As plantar flexion to 10—15° was used in most cases it was sometimes necessary to build up the heel slightly Thereafter the patient was allowed to train walking gradually without crutches The plaster was removed 4—7 weeks after operation and the patient was given a cork heel 1 2 or 3 cm thick to wear inside the heel of the shoe for the first two weeks Remedial gymnastics consisting of active exercises of the ankle joint and strengthening exercises of the lower leg and thigh

muscles, were started on the day of plaster removal They were continued until the range of movement in the talocrural joint was normal after 1—2 months The patients returned for outpatient check-ups 1—2, 3, and 12 months after plaster removal

Complications

No serious complications occurred Apart from transient wound secretion without infection (case 19) and slight irritation of the skin over an area of one cm due to a loosened catgut suture (case 5), all the operation wounds healed by first intention In 1 case (no 13) a subcutaneous haematoma or seroma developed after removal of the plaster and had to be punctured four times However, this did not prevent the patient from starting gradual training 4 months after operation Some tightness of the gliding tissue round the Achilles tendon and the operation scar was noted in 1 case (no 4) for the first 4 months after removal of the plaster A relatively slight tenderness over the grafted area was present for the first few postoperative months in some of the plastic-repair cases

CASE 8 Dorsal — medial rupture

a) Rupture ends enclosed in hardened callous granulation tis ue incision for some dis a ce in the mid line

b) After excis on of granulat on tissue and exposure of the d stally rounded off and the pr x mally pl t rupture end

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CASE 11 Medial rupture
c) Lateral *intact* tendon port on and medial rupture ends

d) Ach lles tendon sutured us g a flap from lateral port on of tendon.

CASE 11 Medial rupture

a) Granulation tissue and hardened tendon like tissue partly removed over rupture ends

b) Rupture ends exposed

CASE 11 Medial rupture
c) Lateral intact tendon portion and medial rupture ends

d) Achilles tendon sutured using a flap from lateral portion of tendon

CASE 19 Central soleus rupture
a) Achilles tendon exposed

b) Incision into palpably harder part

CASE 19 Central rupture
c) Central cystic cavity with granulation tissue haemorrhages and fibrin deposits

d) Central rupture ends after excis on of g anulat on tissue

CASE 19 Central soleus rupture
a) Achilles tendon exposed

b) Incision into palpably harder part

CASE 18 5 day old central — medial rupture

CASE 22 Mult ple small medial ruptures

CASE 10 Transverse rupture through the whole lateral tendinous portion of gastrocnemius

CASE 15 Rupture of soleus portion rupture ends rounded off distally about 1 cm from insertion of Achilles tendon on calcaneus

CASE 18 5 day old central — medial rupture

CASE 2 Multiple small medial ruptures

CASE 22 Medial rupture Plastic repair with plantaris longus tendon

CASE 24 Sutured rupture ventrally in lateral portion of gastrocnemius also slightly involving tendinous portion of soleus

Kolb & Salem (1953) report that in their series of 2 operatively and 2 conservatively treated cases of partial Achilles tendon rupture relief of symptoms and normal tendon function were obtained in the two operation cases in spite of transient fistula formation With the conservative treatment the end result was satisfactory in 1 case but as far as can be judged this patient had a rupture of the gastrocnemius aponeurosis — "tennis leg In the other case in which the rupture involved the free portion of the Achilles tendon fatigability muscle atrophy and tenderness on palpation were still present 4 years after the injury

Conservative treatment

In the present series 13 patients had been treated conservatively for 6—18 months Rest for 2—6 months and in 3 cases immobilization in plaster for 3—4 weeks had not led to improvement Nor had X ray and short wave treatment seemed to improve the condition Local steroid and heparin injections had caused only temporary alleviation of the symptoms Every form of increased activity caused increased pain and swelling of the Achilles tendon

Operative treatment

The length of stay in hospital was 3—7 days The results after this p riod of time will be s en in Tables X and XI The disability period was wholly dependent upon the patient s occupation Three young university students were able to resume studies within 1—2 weeks after operation Three office clerks returned to work after 3 weeks wearing walking plaster Six patients returned to work within 6—7 weeks after removal of the walking plaster Another 6 patients with more strenuous and active type of work returned to it within 2 months Five patients with heavy or highly active type of work were unable to return to work for 3—5 months The oldest patient (aged 65 no 10) resumed half time work within 2 months

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4

TABLE XI

Results

Function	1—2 wk	3—4 wk	6—7 wk	2 mo	3—5 *mo*	6—11 *mo*	1 yr	Total
Return to work	3	3	6	6	6			24
Walking on flat ground			14	10				24
Commenced athletic exercises			1	14		9		4
Complete recovery				12		9	3	4

but, because of the special nature of his occupation, was not able to resume full-time work until 5 months after operation

The ability to walk on flat ground which of course is essential in most normal activities, was recovered within 7 weeks in most and within 2 months in *all* the cases

In the group of champion athletes all, excluding 2, resumed training activities in running, football, and ice hockey Patient no 22 was able *to do high jumps of 1 80 m but after hard sprint training he had diffuse* pain from the non operated portion of the Achilles tendon EMG at several check ups showed no abnormalities, however Patient no 14 did not resume his training activities, but the main reason was that he gained weight during the long period of rest and partly lost interest in champion athletics All the patients in the athlete group resumed their sports activities, such as competing in the Vasa Ski Race, long distance running orienteering gymnastics football, and handball

Half the patients had fully recovered, subjectively and objectively, within 2 months of the operation and all of them had done so within 1 year

Case 2 is an example of the ability of the Achilles tendon to take great loads Once or several times each season for 3½ years this patient returned after periods of hard training with symptoms *of over exertion in the form* of synovitis of the knee joint tenobursitis alternatingly of the right and the left trochanter and ankle sprain but without any complaints of *trouble from the* Achilles tendon after operation Patient no 8 completed a 30 km competitive cross-country race 5 months after operation without any adverse reaction from the Achilles tendon

It will be seen from the account of the results that the forms of con servative treatment used produced no beneficial effects As was men tioned under Treatment conservative treatment by rest and heat may be

justified in cases in which the rupture is judged to be very small If the result is not satisfactory or if such treatment is clearly unlikely to succeed op ration should be performed

The operative methods that were tried in these patients led to complete healing in all the cases within a reasonable period of time With th above said exceptions the author therefore recommends operative treatment of partial rupture of the Achilles tendon

Summary

Subcutaneous partial rupture of the Achilles tendon has been regarded as an unusual injury Many authors have questioned its existence Only in 3 or 4 of the published cases of partial Achilles tendon rupture can the diagnosis be considered confident During a short period of time (1964—1967), however, using a new method of examination (by electromyograhy) I have been able to diagnose and treat by operation 24 such cases at the Department of Surgery, Serafimerlasarettet, Stockholm

Subcutaneous partial rupture of the Achilles tendon refers here to a tear of a varying number of fibres in the free portion of the Achilles tendon most of the fibres usually remaining intact Clinically, the partial Achilles tendon rupture can be differentiated from complete rupture by Thomp son s test — manual compression of the triceps-surae muscle belly — in that plantar flexion of the foot does not occur if the rupture is complete Absence of this reflex is pathognomonic for complete rupture of the Achilles tendon

The present series comprises 24 patients who had undergone operation for the injury at least 1 year previously All of them engaged in some form of sport and the majority had sustained the injury during sports activities The patients can be divided into two age groups one of 19—29 years, in cluding champion athletes alone, and one of 38—65 years, comprising various kinds of non champion athletes and including the only woman patient

Of the aetiological factors described in the literature steroid injections and traumata played a part in this series of cases The steroid injections were probably of no direct aetiological significance they might have played a part by relieving the patients of the symptoms attending a small rupture or some other injury of the Achilles tendon and so allowed in creased weight bearing on the tendon thus being concerned in causing the clinically manifest rupture

The nature of the trauma was analysed and it was found that the pa tients could be divided by the causal violence into one group (14 cases) in which the partial rupture had occurred at running and one group (10 cases) in which the insult was due to slipping or the like The earlier

theories proposing that the subcutaneous complete Achilles tendon rupture occurs in athlete during p riods of inactivity could not be verified in the group of champion athletes with partial ruptures who were all in their most active periods of athletics

The histological changes both in the champion athlete and in the athlete group were characterized by devitalized tendon tissue with altered collagen stainability frayed fibrous structure to which attached granulation tissue converted into more or less tendon like connective tissue Acute inflammatory cell infiltration was s en in 7 cases and chronic in flammatory cell infiltration in all the 24 cases The histological changes associated with a partial rupture of the Achilles tendon may be defined as devitalization of tendon tissue in which the collagen fibres in places have been replaced by granulation tissue

The diagnosis was based on the case history clinical examination X ray examination and electrophysiological examinations

Data concerning lengthy periods of hard training on surfaces that lead to great demands being placed on the Achilles tendon are of great im portance Newly added items on the training programme and any in juries are analysed Besides swelling tenderness stiffness and pain on weight bearing which also occur in tendinitis the patients complained of stabbing jarring or pricking pain in the tendon on suddenly increased activity and of weakness in the calf muscles The pain and the weakness are probably symptoms specific to partial Achilles tendon rupture Eight patients also reported a sensation as of a tear or an audible snap in the tendon region

The clinical examination with the patient standing on his toes placing equal weight bearing on both forefeet showed more or less distinct muscle atrophy (14 cases) of one or both of the gastrocnemius bellies and reduced muscle tone there Increased dorsal extension in the talocrural joint as a sign of lengthening of the muscle and tendon and palpable dents or small defects in the tendon contour should give rise to suspicion of partial Achilles tendon rupture

X ray examination was performed in 19 cases and showed the following changes 1) Local more or less extensive thickening of the tendon (16 cases) 2) tendon contour less distinct than normal and irregularly outlined against the fatty space (10 cases) and 3) infiltration into the soft tissue space (11 cases) Owing to this infiltration a change had also occurred in the Kager triangle which was seen symmetrically narrowed and re duced in comparison with that on the con ralateral uninjured side

The electrophysiological examinations showed

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turn d to work within 2 months The ability to walk on flat ground was recovered within 7 weeks in most and within 2 months in all the cases All but 2 of the champion athletes resumed full training but these 2 carry on relatively high sports activities as do all the athletes Half the patients had fully recovered subjectively and objectively within 2 months and all of them had done so within 1 year

1) Reduction of the amount of motor unit activity in that part of th muscle with ruptured tendon,

2) Increased H-reflex response in cases of rupture of the soleus tendon in other cases normal H-reflexes,

3) Shortened contraction time in cases of rupture of the soleus tendon Increased contraction time and change of the configuration of the contraction curve in cases of rupture of the gastrocnemius tendon

As regards the differential diagnosis, the partial Achilles tendon rupture can be confused with complete rupture, tendinitis, peritendinitis, calcaneal bursitis, periostitis and insufficiency fractures of the fibula or tibia In most cases the clinical and the electrophysiological examinations will help in differentiating with certainty a partial rupture from the above-said conditions

Out of the 24 patients, the majority (13 patients) had undergone long term (6—18 months) conservative therapy consisting of rest, short wave, ultrasonic-wave, and X-ray treatment antiphlogistics (*Tanderil®*, *Butazolidin®*), local steroid and heparin injections, and immobilization in plaster without any noticeable effect

The aim of the operative treatment was to restore the muscle-tendon relation so as to re establish as near as possible normal function After exposure of the Achilles tendon with a medial curved incision and division of the peritenon, the rupture site could be clearly seen in 17 cases In 7 cases the rupture site could not be located until after longitudinal incision of the Achilles tendon over a suspected section with palpable softer or firmer parts and in some instances fusiformly thickened After the rupture site had been located granulation tissue and devitalized tendon tissue was excised The continuity of the tendon was then restored by various methods namely end to end suture (8 cases) side-to-side suture (7 cases) suture and plastic repair with a flap (5 cases) and suture and plastic repair with plantaris-longus tendon (4 cases)

Postoperatively the foot plus the lower leg was immobilized in plaster with the foot plantar flexed for 3 weeks Thereafter the sutures were removed and the patient wore walking plaster for another 3 weeks Active exercises were started immediately after the operation and were continued after plaster removal until the range of movement in the talocrural joint was normal

The disability period varied from 1 week to 5 months It was wholly dependent on the patient s occupation The majority (18 patients) re

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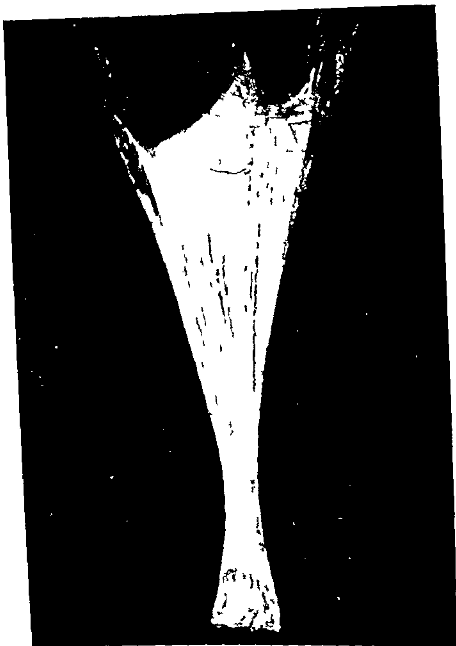


Fig 8

Right Achilles tendon The tendon fibres from the medial gastrocnemius belly descending distally follow an increasingly lateral course toward the insertion on the calcaneus where they make up the lateral part of the Achilles tendon The medial segment of the Achilles tendon is at the insertion made up of tendon fibres from the soleus component This accounts for the rotation which is characteristic of the course of the Achilles tendon fibres and which has been described by Cummins (1949) and Rosate (1964) Centrally the Achilles tendon is made up mainly of soleus fibres Ventrally its medial segment is made up of soleus fibres and its lateral segment of fibres from the lateral gastrocnemius See further the schematic drawings (after Rosate) in the cas report

CASE 2 A 25 year-old policeman and skier who for the last 17 months had had recurrent bursitis myositis of the gastrocnemius and achillotendinitis on the left si e

T eatment Rest, an antiphlogistic (Tanderil®) local application of Buta zol d ne ointment five injections of heparin and six of a steriod only two of the latter being given in the Achilles tendon itself and its in ertio n The last injection gi en 3 months before the trauma

T auma On pressing his right foot down hard for support while grappling with an unruly drunkard he had experienced intense sharp pain in the Achilles tendon of that foot

S bjectively Able to walk but rising on the toes painful

Ob ect ely —3 cm above insertion Achilles tendon th cker ventrally ten derness on palpation and slight depression of tendon contour 10 cm above insertion Marked atrophy and impaired tone of lateral belly of gastrocnemius

X ay Shadow of cal ium deposit immed ately above the calcaneus (calcifica t on in haematoma)

P eope t e E M G Voluntary acti ity much sparser laterally than medially

Oper t on (6 weeks after trauma) Tranverse an l long tudinal rupture of lateral part of tendon from 3 cm to 10 cm abo e insertion Excision with end to-end suture (side to-side)

H stologic lly Dev tali ed tend nous tissue without areas of stainable en doplasm Sl ght ingrowth of granulat on tissue Areas of sl ght perivascular inflammation

Postoper t ve E M G (3 months) No def nite abnormalit es

Outpatient ch ck up (3 months) Us ng an arch support because of some anter or arch trouble Achilles tendon felt normal Occasionally sl ght ten derness Operat on scar normal Tendon function normal

Retu n to work 3 months

O tp t e t ch ck up (7 months) Syno tis due to local o er exertion of right knee jo nt after intensi e running exercise Achilles tendon normal

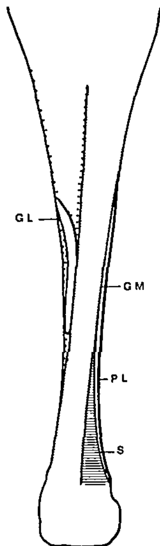
Outpatie t check up (1 year and 7 months) Trochanteric tenobursitis on left side after long-d stance running (30 km) Achilles tendon normal on palpation

R sult Fully act e throughout the racing e sons 1—3 years after opera tion Belongs to the Stockholm top-class athletes District champ on Took part in th Lid ngo race (cross country runn ng 30 km) runs for practice – 2½ hours three t mes a week skis 50 km without any trouble with Achilles tendon

GM

PL

S



CASE 1 A 21 year old engineer and medium distance runner who before the trauma had had tendinitis of the left Achilles tendon of 3 months duration

Trauma (6 months before operation) At the spurt in a 3000 metre race he felt a snap in the region of the left calf He rested from training activities for 2 months On stepping on a threshold he felt the snapping again in the region of the left Achilles tendon

Treatment Local injection of a steroid just over 2 months after first trauma an antiphlogistic (Tanderil®) and rest no response

Subjectively (6 months after trauma) No discomfort in daily life the slightest effort to increased activity caused pain and tenderness of Achilles tendon Training impossible

Objectively Swelling and tenderness on palpation 5 cm above insertion of tendon Marked atrophy impaired muscle tone and tenderness on palpation over lateral belly of gastrocnemius

Preoperative E M G not performed

Operation (6 months after trauma) Oblique rupture just over 10 cm above insertion through lateral portion of tendon to border of medial part Granulation tissue found in the gap Excision with end to end suture

Histologically Devitalized tendon tissue without areas of stainable endoplasm Collagen frayed and decolourized Ingrowth of unspecific granulation tissue

Return to work 7 weeks

Postoperative E M G (2½ months) Voluntary activity sparser than normal No difference between medial and lateral bellies of gastrocnemius

Outpatient check up (4½ months) Subjectively no great discomfort He trained 5 times a week running maximally 10 km Objectively adequate function of tendon

Postoperative E M G (4½ months) Voluntary activity greatly increased but slight asymmetry between lateral and medial bellies of gastrocnemius

Outpatient check up (14 months) Subjectively no complaints Training 6 times a week Interval — running 200—800 metres Long distance running maximally 20 km Objectively operation wound healed normally the atrophy of lateral belly of gastrocnemius barely observable

Postoperative E M G (14 months) Normal

Result (4 years after operation) No troubles whatsoever with Achilles tendon Training regularly 5 times a week for fast and long distance running over 10—20 km

G L = Gastrocnemius lateralis
G M = Gastrocnemius medialis
S = Soleus
P L = Plantaris longus

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X y Shadow of calcium deposit immediately above the calcaneus (calcification in haematoma)

P eope ative E.M G Voluntary activity much sparser laterally than medially

Operati n (6 weeks after trauma) Transverse and longitudinal rupture of lateral part of tendon from 3 cm to 10 cm above insertion Excision with end to end suture (side to side)

Hist logically Devitali ed tend nous tissue without areas of stainable endoplasm Sl ght ingrowth of granulation tissue Areas of sl ght peri ascular inflamm tion

Postope at e E M G (3 months) No definite abnormal ties

Outpatient check up (3 months) *Using* an arch support because of some anterior arch tro ble Achilles tendon felt normal Occasionally slight tenderness Operat on scar normal Tendon function normal

Retu n to wo k 3 months

Outpati nt check up (7 months) Syno itis due to local over exertion of right knee joint after intensi e running exercise Achilles tendon normal

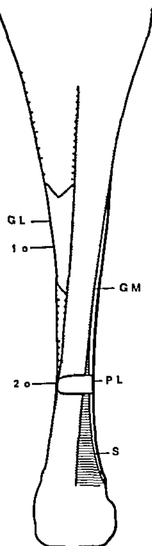
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GM

P L.

S



CASE 3 A 46 year old electrician who frequently had to climb ladders

First trauma (1½ years before operation) Sustained a blow of a reinforcing iron bar against right Achilles tendon after which he had troubles in the form of increasing tenderness and thickening over the tendon for 1½ years

Treatment An antiphlogistic (Tanderil®) short wave treatment After local steroid injection within 6 months of the trauma the swelling diminished

Subjectively (1½ years after trauma) Difficulties in rising on his toes and climbing ladders Felt stabbing pain in the tendon on getting on to a chair

Objectively Right Achilles tendon thinner than left one because of depression in tendon contour laterally and above insertion Dorsal extension in talocrural joint increased to 10 more than normal Generalized atrophy of gastrocnemius

Preoperative EMG Volitional activity much less laterally than medially

On the waiting list for operation of lateral partial rupture of Achilles tendon

Second trauma (6 weeks after objective examination and 2 weeks after EMG) Stumbled on a board at building site and felt something like a violent blow from behind

Objectively Complete rupture of tendon with diastasis 4—5 cm above insertion Thompson s test did not elicit plantar flexion of foot

Operation (1½ years after first trauma and on the day after second trauma) 1) Old rounded off partial rupture of lateral portion of tendon proximal end of rupture retracted just over 5 cm from distal end which was slightly more irregularly rounded ?) Fresh rupture with haemorrhages and torn tendon fibres through medial and soleus portions of tendon Plastic repair by Silfverskiold s method (modified)

Histologically Devitalized tendon tissue with altered *collagen stainability and* poorly visible fibrous structure

Postoperative EMG (7 weeks) Sparse volitional activity in bursts mainly medially

Return to work 11 weeks

Outpatient check up (13 weeks) Normal range of movement and tendon function Able to rise on his toes for the first time in just over 1½ years

Postoperative EMG (3½ years) Fully normal

Result (3½ years after operation) Able to climb ladders etc without difficulties no trouble with Achilles tendon

CASE 4 A 29 year-old engineer and ice hockey player with a 3 year history of recurrent tendinitis of left Achilles tendon

T eatment Heparin injection Local steroid injection 4 months and 2 months before trauma led to temporary impro ement An antiphlogistic (Tan deril®)

Fi st t auma (7 weeks before operation) During an ice hockey match he pulled up suddenly — to a oid an object on the ice — and felt a jarring pain in left Achilles tendon

Sub ectively (5 weeks after trauma) Swelling and pain on walking up and down stairs unable to rise on his toes

Objectively M nor defect in tendon contour laterally —3 cm above inser tion with a rounded off thickening d stally which was tender to palpa tion Dorsal extension in talocrural jo nt increased to a few degrees more than normal

P eope ative E M G Decreased vol tional activity laterally

On u t g list for operation

Seco d t auma (8 days after exam nation) Tripped on stairs and felt a tear in Achilles tendon

Obje tively A distinct depress on in Achilles tendon laterally 3—4 cm abo e insertion but tendon intact medially Thompson s test ga e plantar flexion

X ay Soft tissue space around tendon was infiltrated

Ope tion (7 weeks after first trauma)

1 Old rounded off rupture laterally in lateral portion of tendon
2 Fresh oblique rupture with haemorrhages in lateral port on of tendon also in olving a small part of medial portion

Plast c repair by S lf erskiold s method (modified)

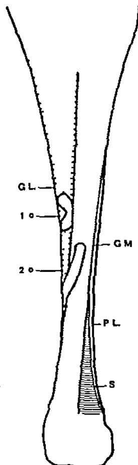
Hist log cally Part ally devitalized tendon tissue and still v tal tendon tissue w th altered collagen stainability and frayed fibrous structure In places tendon transformed into granul t on tissue with sparse unspecif c inflam matory cell infiltration

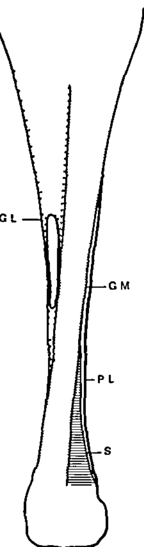
Retu n to u k Resumed his stud es 10 days after operation

Post pe tive E M G (4 months) Normal

Outpatient check up (6 months) Some tightness in gliding tissue around Achilles tendon and operation scar for fi st 4 months after removal of pl ster Operat on scar normal

Result Fully act e at ice hockey every season for 3 years after operation and has suffered no tendon troubles whatsoe er





CASE 5 A 42 year old engineer and allround athlete who 1 year before the trauma had been given a local injection of a steroid for tendinitis of the left Achilles tendon after which he had been free from symptoms for 1 year

Trauma (12 months before operation) On sudden start at —20 C in the Vasa Ski Race (85 km) he felt a burning pain in left Achilles tendon Persisting trouble with tendon

Treatment Six heparin and 9 local steroid injections An antiphlogistic (Tanderil®) ultrasonic waves and rest for 2 months had no effects over a period of 11 months

Subjectively (11 months after trauma) Pain in Achilles tendon on movement tendon felt swollen and clotted in the night no trouble in his daily activities

Objectively (11 months after trauma) Thickening about 10 cm above insertion of tendon with tenderness on palpation over this area Atrophy of 1 5 cm of calf but no difference between lateral and medial bellies of gastrocnemius Slightly increased dorsal extension

Preoperative E M G Voluntary activity fairly good but somewhat less laterally though not sufficiently so to give rise to suspicion of rupture on the basis of E M G

Operation (12 months after trauma) Fusiform thickening 6—7 cm above insertion with a laterally darker tendinous streak one cm in length and adhesions ventrally in this area Exposure revealed a cystic cavity 5 cm long with a few thin ruptured tendon fibres the walls showed partly obliterated tendon structure Excision up to normal tendon tissue side to side suture

Histologically Areas of split devitalized tendon tissue with newly formed tendon like granulation tissue

Outpatient check up (4 weeks) Plaster removed after 4 weeks Operation wound slightly irritated over an area of one cm Catgut suture which had loosened was removed Pain in plantar aponeurosis Arch support for pain in calcaneus spur

Return to work 6 weeks after operation

Outpatient check up (6 weeks) Subjectively no complaints No tenderness on palpation over operating field Operation wound normal

Postoperative E M G (6 weeks) Normal

Outpatient check up (6 months) In full training but after running for about 1½ hours he noticed symptoms of tenobursitis of knee joint but had no troubles whatsoever with Achilles tendon

Outpatient check up (7 months) After cross country running he had stabbing pain in region of right calf small partial rupture of gastrocnemius

Postoperative E M G (7 months) Completely normal

Result (2 years and 9 months) Fully active in skiing and training without any troubles whatsoever

CASE 6 A 9 year old electrician football bandy and ice hockey player with a h story of recurrent tendinitis of both Achilles tendons for 3 years Local steroid inject on 1 year before the trauma had relieved the symptoms during the bandy and ice hockey season As the condition was aggravated after football training practice E M G was performed but showed no definite abnormalities

Trauma (9 months before operation and 2 weeks after abo e said E M G) Stumbled at work and felt a sharp sudden pain in right Achilles tendon

Treatment Short wa e and X ray an antiphlogistic (Tanderil®) Hirudoid and Butazolid ne ointment heparin injections local steroid injection enabled the pat ent to play bandy and ice hockey in the w nter but not football

Subjectively (8 months after trauma) Sharp pa n in right Achilles tendon on increased activity He had to walk with st ff foot

Obj cti ly *La erally a good 2 cm abo e insertion a tear was suspected in* Achilles tendon contour which proximal to th s site was thickened and tender to palpation

Preope t e E.M G Interpretation difficult possibly slightly sparser voluntary act ty in the lateral part of the right gastrocnemius

X ay Right Ach lles tendon slightly th ckened 5 cm above calcaneus

Ope tion (8 months after trauma) Peritenon adherent to subcutis Laterally 3—5 cm abo e insertion se eral small ruptures relati ely superficially Plast c repair with a flap from medial common aponeurosis

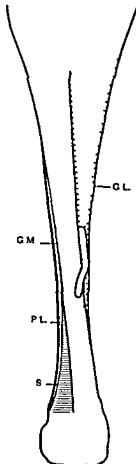
H stolog c lly 1) Peritenon with newly formed granulation t ssue of tendon like type 2) Devitalized tendon tiss e and newly formed tendon like gra nulat on tissue

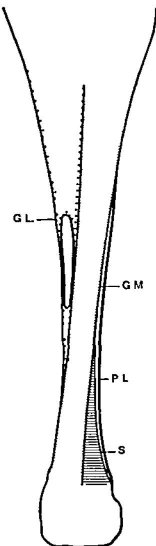
Retu n to work months

Outp tient check up ($3^1{}_2$ months) At first some stiffness in the morning Some tenderness o er operation area Operation wound normal He had commenced training

P stop ati e E M G ($3^1{}_2$ months) No definite pathological changes No asymmetry

Result (years after operation) Played n a football match 5 months after ope ation Had been fully active in football and regained h s old sw ftness No troubles with right Achilles tendon but had had an injury of collateral l gament in right knee t ochanter tenobursitis and partial semimembrano s rupture Operation wound sat sfactory No tenderness on palpat on R ght Ach lles tendon slightly thicker than left one Fully satis actory muscle tendon f nction Normal range of mo ement in ankle joint





CASE 5 A 42 year old engineer and allround athlete who 1 year before the trauma had been given a local injection of a steroid for tendinitis of the left Achilles tendon after which he had been free from symptoms for 1 year

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Subjectively (11 months after trauma) Pain in Achilles tendon on movement tendon felt swollen and clotted in the night no trouble in his daily activities

Objectively (11 months after trauma) Thickening about 10 cm above insertion of tendon with tenderness on palpation over this area Atrophy of 1 5 cm of calf but no difference between lateral and medial bellies of gastrocnemius Slightly increased dorsal extension

Preoperative E M G Voluntary activity fairly good but somewhat less laterally though not sufficiently so to give rise to suspicion of rupture on the basis of E M G

Operation (12 months after trauma) Fusiform thickening 6—7 cm above insertion with a laterally darker tendinous streak one cm in length and adhesions ventrally in this area Exposure revealed a cystic cavity 5 cm long with a few thin ruptured tendon fibres the walls showed partly obliterated tendon structure Excision up to normal tendon tissue side to side suture

Histologically Areas of split devitalized tendon tissue with newly formed tendon like granulation tissue

Outpatient check up (4 weeks) Plaster removed after 4 weeks Operation wound slightly irritated over an area of one cm Catgut suture which had loosened was removed Pain in plantar aponeurosis Arch support for pain in calcaneus spur

Return to work 6 weeks after operation

Outpatient check up (6 weeks) Subjectively no complaints No tenderness on palpation over operating field Operation wound normal

Postoperative E M G (6 weeks) Normal

Outpatient check up (6 months) In full training but after running for about 1½ hours he noticed symptoms of tenobursitis of knee joint but had no troubles whatsoever with Achilles tendon

Outpatient check up (7 months) After cross country running he had stabbing pain in region of right calf small partial rupture of gastrocnemius

Postoperative E M G (7 months) Completely normal

Result (2 years and 9 months) Fully active in skiing and training without any troubles whatsoever

CASE 8 A 40 year old electrical fitter and allround athlete

T auma (14 months before operation) While cycling up a 400-metre long hill standing on the pedals he felt violent pain in right Achilles tendon Before this incident he had had a period of training running ?400 km and cycl ng 100 km After trauma tendon painful for 14 months

Treatment He arin and stero d injections on 9 occas ons An antiphlogistic (Tanderil®) Immobilization in plaster and 3 weeks of hospital care

S bjectively Stabbing pain on increased activity but also ach ng at rest a centuated after an effort to run in the Vasa Ski Race after ski ng 50 km he was unable to walk

Object vely R ght Achilles tendon twice as thick as left one with fusiform thickening 3—4 cm above insertion intense tenderness on palpation o er this area and possibly slight incongruence of contour med ally and dor ally Dorsal extension in talocrural joint increased to 15 more than normal

P eoperative E M G No definite abnormalit es but slight d fference in com parison with E M G 6 weeks pre iously Reduced voluntary activity in the med al part of gastrocnemius

X ray *Right A hill s tendon twice as thick as left one uncl arly outlined* soft tissue infiltrat on

Ope ation (14 months after trauma) Dorsally Achilles tendon furrowed centrally with small haemorrhages and enclosed in hardened callous gra *nulat on tissue Dorsal m dial partial rupture with rounded off rup ure* ends End to end suture and plastic repair with a flap turned o er from lateral normal tendon fascicle

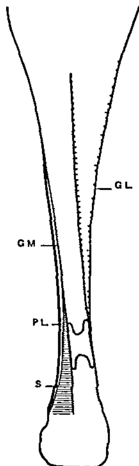
Histologically Partly dev talized tendon tissue w th decolourized collagen and *h re and th re form t on of granulation tissue*

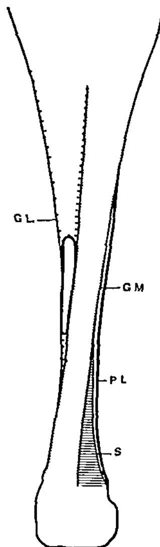
Post perati e E M G (6 weeks) Normal

Retu n to wo k 6 weeks after operation

Outp t e t check up (5 months) He had just completed the Lidingo Race *cro s o ntry runn ng 30 km w thout any troubles with Achilles tendon* Operat on scar normal No tenderness on palpat on

Result (1 2 years after operat on) Another L d ngo Race and two Vasa Ski Races fte ope ation Trained r nning on hard road the following sea ons *1600—1750 km Employed as a gymnast s master* on duty for 7 hours e ery day No t oubl hatsoe er w th Ach lles tendon





CASE 7 A 51 year old carpenter and footballer

Trauma (1 year before operation) While kicking a football against a brick wall and joggling he felt intense pain in right Achilles tendon and then had difficulties in walking

Treatment Two local steroid injections 1 week after trauma Rest an anti phlogistic (Tanderil®) Immobilisation in plaster for 3 weeks Elastic bandag

Subjectively (11 months after trauma) Tenderness and difficulty in walking up and down stairs

Objectively Thickening with fluctuation and tenderness on palpation 3—4 cm above insertion of tendon Muscle atrophy with reduced tone laterally Dorsal extension in ankle joint slightly increased

Preoperative E M G Voluntary activity somewhat less laterally

X ray Achilles tendon slightly thickened over an area about 4 cm in length 2 cm proximal to calcaneus

Operation (1 year after trauma) Fusiform thickening 3—4 cm above insertion of opaque appearance laterally Longitudinal incision in softer part revealed a cystic cavity in lateral portion of tendon with granulation tissue and partly obliterated tendon structure Excision end to end suture

Histologically Devitalized tendon tissue with frayed fibrous structure poor stainability in endoplasm reas and altered collagen stainability To this tissue attached streaks of newly formed granulation tissue rich in collagen and of finely streaked and wavy structure which differed from that of normal tendon tissue

Outpatient check up (2 months) Occasionally slight pain Operation scar normal Strength in foot and lower leg not quite normal return to work therefore postponed

Outpatient check up (2½ months) Subjectively and objectively virtually free from symptoms

Return to work 2½ months after operation

Postoperative E M G (4½ months) Normal

Result (2 years after operation) Climbs scaffolds Heavy weight bearing on Achilles tendon — wheeling loads of mortar Plays tennis No trouble whatsoever with the tendon

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Treatment Heparin and steroid injections on 9 occasions An antiphlogistic (Tandet ®) Immobilization in plaster and 3 weeks of hospital care

Subjectively Stabbing pain on increased activity but also aching at rest accentuated after an effort to run in the Vasa Ski Race after skiing 50 km he was unable to walk

Objectively Right Achilles tendon twice as thick as left one with fusiform thickening 3—4 cm above insertion intense tenderness on palpation over this area and possibly slight incongruence of contour medially and dorsally Dorsal extension in talocrural joint increased to 15 more than normal

Preoperative EMG No definite abnormalities but slight difference in comparison with EMG 6 weeks previously Reduced voluntary activity in the medial part of gastrocnemius

X-ray Right Achilles tendon twice as thick as left one unclearly outlined soft tissue infiltration

Operation (14 months after trauma) Dorsally Achilles tendon furrowed centrally with small haemorrhages and enclosed in hardened callous granulation tissue Dorsal medial partial rupture with rounded off rupture ends End to end suture and plastic repair with a flap turned over from lateral normal tendon fascicle

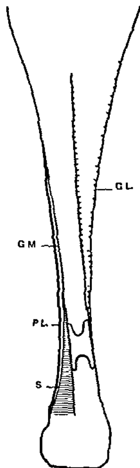
Histologically Partly devitalized tendon tissue with decolourized collagen and here and there formation of granulation tissue

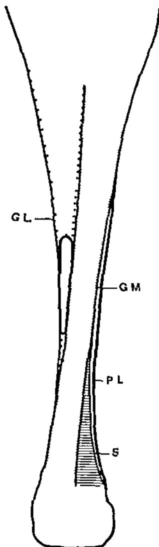
Postoperative EMG (6 weeks) Normal

Return to work 6 weeks after operation

Outpatient check up (5 months) He had just completed the Lidingo Race cross country running 30 km without any troubles with Achilles tendon Operation scar normal No tenderness on palpation

Result (1½ years after operation) Another Lidingo Race and two Vasa Ski Races after operation Trained running on hard road the following seasons 1600—1750 km Employed as a gymnastics master on duty for 7 hours every day No trouble whatsoever with Achilles tendon





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Preoperative E M G Voluntary activity somewhat less laterally

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Outpatient check up (2½ months) Subjectively and objectively virtually free from symptoms

Return to work 2½ months after operation

Postoperative E M G (4½ months) Normal

Result (2 years after operation) Climbs scaffolds Heavy weight bearing on Achilles tendon — wheeling loads of mortar Plays tennis No trouble whatsoever with the tendon

CASE 10 A 65 year-old colonel and athlete who had had medial tendinitis of left Achilles tendon for 4 months E.M G negative After local steroid injection medially only about 3—4 cm above insertion he had been symptom free until injury occurred

Trauma Stepping side ways on his foot he slipped on the kerb and felt stabbing pain in the calf

Subjectively (3 days after trauma) Unable to rise on the toes because of pain

Objectively Tenderness on palpation and oedema about 10 cm above insertion a dent in tendon contour laterally Dorsal extension in talocrural joint increased to 5—10 more than normal

Preoperative E M G Volitional activity much less in left than in right gastrocnemius muscle Asymmetry with fewer motor units laterally than medially Prolonged contraction time

X ray Left Achilles tendon thickened

Operation (2 weeks after trauma) Haemorrhages and partial rupture laterally 10 cm above insertion rupture involved greater part of lateral tendon fascicle with diastasis of 3—4 cm between rupture ends distally ensheathed by tendinous callus Excision end-to-end suture Medially tendon structure fully normal

Histologically Devitalized tendon tissue showing altered collagen stainability and frayed fibrous structure Slight tendency to formation of granulation tissue Signs of fibrin exudation around areas of devitalized tendon tissue

Outpatient check up (2 months and 10 days after operation) Subjectively virtually symptom free Operation scar normal

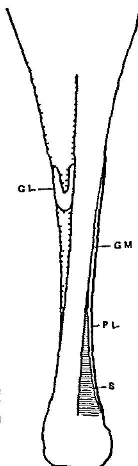
Return to work 50 % 2 months after operation

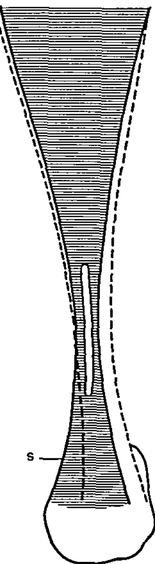
Outpatient check up (5 months) A tender part laterally 15—20 cm above insertion had troubled him for a month but had cleared up at time of examination Operation scar normal No tenderness on palpation Normal range of movement in ankle joint

Return to full time work 5 months after operation

Postoperative E M G (5 months) Fully normal

Result (2 years after operation) Walked fast every day for 1½—2 *hours* without stopping half running occasionally Light physical exercises No trouble with Achilles tendon after operation





CASE 9 A 54 year old woman engineer and athlete who had been operated on for subcutaneous complete rupture of left Achilles tendon in 191(

Trauma During a cross country run she slipped on a stone and felt a sharp pain in right Achilles tendon

Treatment Rest

Subjectively Weight bearing painful difficulty in walking up and down s airs Stabbing pain on increased activity Aching at rest

Objectively (1 months after trauma) Diffuse thickening of Achilles tendon 3—4 cm above insertion and tenderness on palpation of this area as well as slightly further proximally After increased weight bearing by walking up and down a flight of stairs the tenderness was localized distinctly laterally

Preoperative E M G Fairly good voluntary activity slightly reduced laterally Shape of contraction curve deviated from normal slightly prolonged dura tion Pathological finding not wholly characteristic but suspected to b evidence of rupture

Operation (1 month after trauma) Achilles tendon seemed to be intact but a longitudinal incision over an area of opaque appearance revealed a cystic cavity with haemorrhages and two torn tendon ends united by granula tion tissue Excision up to healthy tendon tissue resulting in a cavity 10—12 cm long Side to side suture

Histologically Partially devitalized tendon tissue with poorly stainable en doplasm areas and reduced collagen stainability Granulation tissue formed in places Minimal inflammatory cell infiltration The continuity of col lagen fibres here and there broken by granulation tissue which indicated the presence of partial rupture

Outpatient check up (2 months) Subjectively no complaints Operation scar normal No tenderness on palpation

Postoperative E M G (2 months) Normal

Return to work Just over ? months after operation

Result During the first 2 postoperative years she was able to carry on various forms of sports downhill skiing physical exercises twice a week with ½ hour of cross country running each time No trouble whatsoever with Achilles tendon

CASE 10 A 65 year-old colonel and athlete who had had medial tendinitis of left Achill s tendon for 4 months E.M.G negati e After local steroid injection medially only about 3—4 cm abo e insertion he had been symptom free until injury occurred

Trauma Stepping sideways on his foot he slipped on the kerb and felt stabbing pain in the calf

Subjectively (3 days after trauma) Unable to rise on the toes because of pain

Objectively Tenderness on palpation and oedema about 10 cm abo e inser tion a dent in tendon contour *laterally Dorsal extension in talocru al joint* increased to 5—10 more than normal

Preoperative E.M.G Vol tional activity much less in left than in right gastrocnemius muscle Asymmetry with fewer motor units laterally than medially Prolonged contraction time

X ray Left Achilles tendon thickened

Oper t on (2 weeks after trauma) Haemorrhages and partial rupture laterally 10 cm above insertion rupture in ol e l greater part of lateral tendon fa sci le with diastasis of 3—4 cm between rupture ends distally ensheathed by tendinous callus Exci ion end to end suture Medially tendon structure fully normal

Histologically Devitalized tendon tissue showing altered collagen sta nability and frayed fibrous structu e Slight tendency to formation of granulation tissue S gns of fibrin exu lation around areas of devitalized tendon tissue

Outpat e t check up (2 months and 10 days after operation) Subjecti ely irtually symptom free Operation scar normal

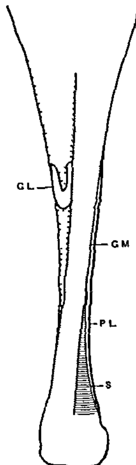
Retu n to wo k 50 % 2 months after operation

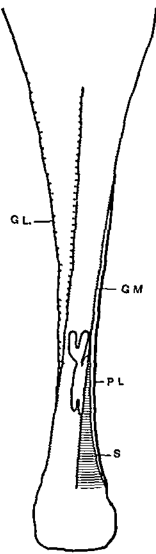
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R turn to full tim work 5 months after operat on

Post pe ti e E.M.G (5 months) Fully normal

Result (years after operat on) Walked fast every day for $1^{1/}$—*2 hou s* w tho t stopping half running occas onally L ght physical exerc ses No trouble with Achilles tendon after operat on





CASE 11 A 44 year old district manager and allround athlete who had had recurrent tendinitis of left Achilles tendon for just over 1 year. Seven months after onset he had been given a local steroid injection: the symptoms had disappeared after 1 week and he had then been symptom free for 6 weeks up to the time of the trauma.

First trauma (3 months before operation). Distortion of right ankle joint with excessive weight bearing on left Achilles tendon.

Treatment. Local steroid injection plus an antiphlogistic (Tanderil®) produced no effect.

E M G (6 weeks after trauma). No abnormalities.

Second trauma (7 weeks before operation). Tripped and made a false step on kerb; felt a violent pain in left Achilles tendon and calf muscle.

E M G. No abnormalities.

Treatment. An antiphlogistic (Tanderil®) plus local steroid injection but only in medial gastrocnemius part which was tender on palpation (tennis leg): tenderness over this region disappeared but pain in Achilles tendon persisted.

Subjectively (1 months before operation). Tenderness over lower part of tendon. Incessant pain on walking. Unable to run more than 50 metres.

Objectively. Soft tissue swelling, tenderness on palpation over tendon and suggested fluctuation medially 5—6 cm above insertion. Atrophy and reduced tone of medial gastrocnemius belly. Slightly increased dorsal extension in talocrural joint.

X ray. Left Achilles tendon thicker than right one. Probably partial rupture.

Preoperative E M G. Slightly reduced voluntary activity in the medial gastrocnemius belly.

Operation (3 months after first trauma). Medially an area of just over 10 cm of Achilles tendon covered with hardened tissue. Exposure revealed three partly oblique tears in medial portion of tendon. Excision, suture plus plastic repair using a flap from lateral portion.

Histologically. 1) Highly sclerosed tendon-like granulation tissue. Slight inflammatory cell infiltration. Centrally yellowish red collagen bundles being rests of old tendon tissue with vascularization. 2) Same as above. Profuse vascularization. Lymphomonocytic infiltrates around vessels. Areas of transition from granulation tissue to newly formed tendon-like connective tissue.

Return to work. 4 weeks.

Outpatient check up (4 months). After walking for 30—45 minutes he had still some pain on medial side: adhesions? Normal range of movement in talocrural joint. Can rise on his toes without pain. No tenderness on palpation.

Postoperative E M G (4 months). Normal.

Outpatient check up (10 months). Started training about 7 months after operation. Competing in orienteering contests almost every other day and never over distances shorter than 7 km. Subjectively no complaints. Very occasionally slight pricking but rapidly passing sensation in Achilles tendon.

Result (2 years). Subjectively and objectively wholly symptom free as regards Achilles tendon. Operation scar normal. No muscle atrophy. Some complaints of pain on movement in right shoulder and elbow when playing tennis.

CASE 1 A 4? year old manager former speedway driver and athelete

Trauma (5 months before operation) Caught his left foot under a stone and was butted on the calf by a vicious ram He felt a violent pa n above the ankle as if something and been broken Interpreted as a muscle sprain

Tre tment Elastic bandage rest

Sub ctively (5 months after trauma) Pa n above le t ankle Difficulty in walk n up and down a flight of stairs Cannot stand on tipto s

Ob ectively Depress on in Achilles tendon contour with palpable diastasis 4 cm in length in lateral part of tendon Medially tendon appeared to be at least partially intact at palpation Atrophy of lateral and medial gastroc nemius Dorsal extension in talocrural joint increased to 15 more than norm l Thompson s test gave plantar flexion of foot though with re duced m s ular strength

X r y Left Achilles tendon much thicker than right one Infiltration in fat in front of Achilles tendon

P eope tive E M G Greatly reduced volitional acti ity laterally possibly also in the soleus

Op ation (5 months after trauma) Hardened tissue enclosed a partial rup ture wh ch involved lateral as well as soleus portions and also part of medial tendon fascicle Centrally a plantaris longus tendon as thick as tip of l ttle finger So as to achieve sat sfatory opposition at suturing the intact medial fascicle was also divided Plastic repair using plantaris ten don and turning down of a flap from medial fascicle

Hist l gically Partially devitali ed tendon t ssue changing nto granulation and newly formed collagen poorer tendon l ke tissue Fairly dense lympho-cytic infiltra es su rounded the essels The surface of some areas was co ered with fibrin f agments

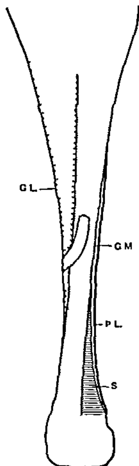
Outpati nt check up (3 months) Subject ely relat ely normal Operation scar normal Relatively slight tenderness on palpation o er s te of repair Normal range of mo ement in ankle joint

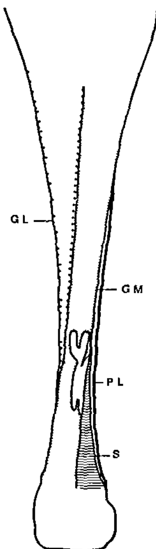
Retu to w k 3½ months after operat on

Post p t E M G planned but not perfo med unt l 2 years after opera t on as the t me did not suit the patie t and the foot d d not trouble him at all

E M G (ye s) Completely norm l

Result (year) 100 % reco ery Fully acti e cycling ski ng and swim ming w thout any t ouble whats ever w th Ach lles tendon





CASE 11 A 44 year old district manager and allround athlete who had had *recurrent tendinitis of left Achilles tendon* for just over 1 year Seven months after onset he had been given a local steroid injection the symptoms had disappeared after 1 week and he had then been symptom free for 6 weeks up to the time of the trauma

First trauma (3 months before operation) Distortion of right ankle joint with excessive weight bearing on left Achilles tendon

Treatment Local steroid injection plus an antiphlogistic (Tanderil®) produced no effect

E M G (6 weeks after trauma) No abnormalities

Second trauma (7 weeks before operation) Tripped and made a false step on kerb felt a violent pain in left Achilles tendon and calf muscle

E M G No abnormalities

Treatment An antiphlogistic (Tanderil®) *plus local steroid injection* but only in medial gastrocnemius part which was tender on palpation (tennis leg) tenderness over thi region disappeared but pain in Achilles tendon persisted

Subjectively (1 months before operation) Tenderness over lower part of tendon In essant pain on *walking* Unable to run more than 50 metres

Objectively Soft tissue swelling tenderness on palpation over tendon and suggested fluctuation medially 5—6 cm above in ertion Atrophy and reduced tone of medial gastrocnemius belly Slightly increased dorsal extension in talocrural joint

X ray Left Achilles tendon thicker than right one Probably partial rupture

Preoperative E M G Slightly reduced voluntary activity in the medial gastrocnemius belly

Operation (3 months after first trauma) Medially an area of just over 10 cm of Achilles tendon covered with hardened tissue Exposure revealed three partly oblique tears in medial portion of tendon Excision suture plu plastic repair using a flap from lateral portion

Histologically 1) Highly sclerosed tendon like granulation tissue Slight inflammatory cell infiltration *Centrally yellowish red collagen bundles being* rests of old tendon tissue with vascularization 2) Same as above Profuse vascularization Lymphomonocytic infiltrates around vessels Areas of transition from granulation tissue to newly formed tendon like connective tissue

Return to work 4 weeks

Outpatient check up (4 months) After walking for 30—45 minutes he had still some pain on medial side adhesions? Normal range of movement in talocrural joint Can rise on his toes without pain No tenderness on palpation

Postoperative E M G (4 months) Normal

Outpatient ch ck up (10 months) Started training about 7 months after operation Competing in orienteering contests almost every other day and never over *distances shorter than 7 km* Subjectively no complaints Very occasionally slight pricking but *rapidly passing sensation in Achilles* tendon

Result (2 years) Subjectively and objectively *wholly symptom free as re*gards Achilles tendon Operation s ar normal No mu cle atrophy Some complaints of pain on movement in right shoulder and elbow when playing tennis

CASE 1 A 4? year old manager former speedway driver and athelete

Trauma (5 months before operation) Caught his left foot under a stone and was butted on the calf by a icious ram He felt a violent pain above the ankle as if something and been broken Interpre ed as a muscle sprain

Treatment Elastic bandage rest

Sub ectively (5 months after trauma) Pain abo e le t ankle Difficulty in walk ng up and down a flight of stairs Cannot stand on tipto s

Objectively Depression in Ach lles tendon contour with palpable diastasis 4 cm in length n lateral part of tendon Medially tendon appeared to be at least partially intact at palpation Atrophy of lateral and medial gastroc nemius Dorsal extension in talocrural joint increa ed to 15 more than normal Thompson s test gave plantar flexion of foot though with re duced mus ular strength

X ay Left Achilles tendon much thicker than right one Infiltration in fat in front of Achilles tendon

P eope t ve E.M G Greatly reduced volitional activity laterally possibly also in the soleus

Operation (5 months after trauma) Hardened tissue enclosed a partial rup ture which nvolved lateral as well as soleus portions and also part of med al tendon fascicle Centrally a plantaris longus tendon as thick as tip of l ttle finger So as to achieve satisfatory opposition at suturing the intact med al fascicle was also d vided Plastic repair using plantaris ten don and turning down of a flap from medial fascicle

H stologically Partially de italized tendon t ssue changing into granulation and newly formed collagen poorer tendon l ke tissue Fairly dense lympho cytic infiltrates surrounded the vessels The surface o some areas was co ered w th f brin fragments

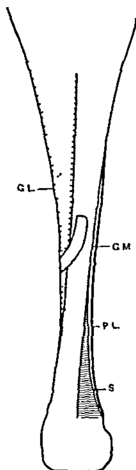
Outpatient heck up (3 months) Subjecti ely relati ely normal Operation scar norm l Relatively slight tenderness on palpation o er site of repair Normal range of mo ement in ankle joint

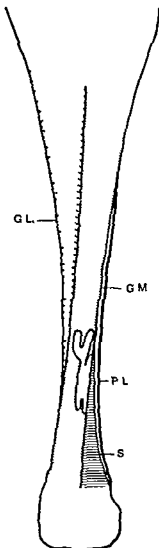
Return to work 3½ months after operation

Po t perative E M G planned b t not performed until ? years after opera t on, as the time did not suit the patient and the foot did not t ouble h m at all

E M G (ye) Completely normal

R s t (years) 100 % recovery Fully acti e cycling skiing and swim m ng without any trouble whatsoe er with Achilles tendon





CASE 11 A 44 year old district manager and allround athlete who had had recurrent tendinitis of left Achilles tendon for just over 1 year Seven months after onset he had been given a local steroid injection the symptoms had disappeared after 1 week and he had then been symptom free for 6 weeks up to the time of the trauma

First trauma (3 months before operation) Distortion of right ankle joint with excessive weight bearing on left Achilles tendon

Treatment Local steroid injection plus an antiphlogistic (Tanderil®) produced no effect

E M G (6 weeks after trauma) *No abnormalities*

Second trauma (7 weeks before operation) *Tripped and made a false step on* kerb felt a violent pain in left Achilles tendon and calf muscle

E M G No abnormalities

Treatment An antiphlogistic (Tanderil®) plus local steroid injection but only *in medial gastrocnemius part which was tender on palpation (tennis* leg) tenderness over this region disappeared but pain in Achilles tendon persisted

Subjectively (1 months before operation) Tenderness over lower part of tendon Incessant pain on walking Unable to run more than 50 metres

Objectively Soft tissue swelling tenderness on palpation over tendon and suggested fluctuation medially 5—6 cm above insertion Atrophy and reduced tone of medial gastrocnemius belly Slightly increased dorsal extension in talocrural joint

X ray Left Achilles tendon thicker than right one Probably partial rupture

Preoperative E M G Slightly reduced voluntary activity in the medial gastrocnemius belly

Operation (3 months after first trauma) Medially an area of just over 10 cm of Achilles tendon covered with hardened tissue Exposure revealed three partly oblique tears in medial portion of tendon Excision suture plus plastic repair using a flap from lateral portion

Histologically 1) Highly sclerosed tendon like granulation tissue Slight inflammatory cell infiltration Centrally yellowish red collagen bundles being rests of old tendon tissue with vascularization *2) Same as above Profuse* vascularization Lymphomonocytic infiltrates around vessels Areas of *transition from granulation tissue to newly formed tendon like connective* tissue

Return to work 4 weeks

Outpatient check up (4 months) *After walking for 30—45 minutes he had* still some pain on medial side adhesions? Normal range of movement in talocrural joint Can rise on his toes without pain No tenderness on palpation

Postoperative E M G (4 months) Normal

Outpatient check up (10 months) Started training about 7 months after operation *Competing in orienteering contests almost every other day* and never over distances shorter than 7 km Subjectively no complaints Very *occasionally slight pricking but rapidly passing* sensation in Achilles tendon

Result (_ years) Subjectively and objectively wholly symptom free as regards Achilles tendon Operation scar normal No muscle atrophy Some complaints of pain on movement in right shoulder and elbow when playing *tennis*

CASE 14 A 4 year old university student and champion long-distance runner He had had trouble with left Achilles tendon for 1½ years clinically diagnosed as achillotenobursitis Local steroid injection in the calcaneal bursa relieved the symptoms and enabled him to run races until he sustained the injury

T ma (1½ years before operation) When training barefooted on a golf course he felt a sudden pain in the region of left Achilles tendon immediately above insertion The pain persisted

Treatment Rest Butazolidine ointment After 5 months a steroid injection was given locally at the calcaneal insertion and after another ½ months into the region of the bursa As no response was noted dimethyl sulphoxide (DMSO) was tried

Subjectively (1 month before operation) Pain and tenderness on increased activity Almost unable to run 50 metres to catch a bus

Objectively Achilles tendon distinctly thicker immediately above insertion and tender to palpation laterally Atrophy of just over 1 cm of triceps surae

Preop rative EMG Volitional activity reduced laterally

X r y Left Achilles tendon twice as thick as right one

Ope ation (1½ years after trauma) Achilles tendon looked normal on the whole but 3—4 cm above insertion there was a slightly uneven and raised section Incision revealed a cystic cavity with two rupture ends and profuse granulation tissue and fibrin End to end suture

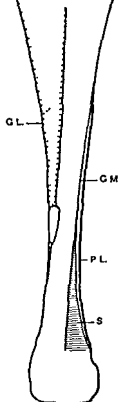
Histol gically Devitalized tendon tissue partly transformed into and infiltrated by unspecific granulation tissue with newly formed tendon like connective tissue Some areas were coated with a fibrin like mass

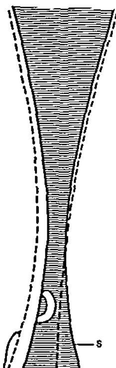
Retu n to w rk 10 days after operation

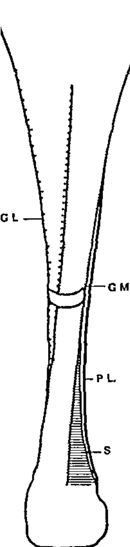
Outpatie t check up (3 months) Subjectively no complaints Operation scar normal Full range of movement in talocrural joint

P stope ative EMG (3½ months) Normal

R lt (years) No troubles with Achilles tendon Training twice a week running 7—8 km He had not resumed competitive sports because of studies among other reasons







CASE 13 A 38 year old engineer and handball player

Trauma During a handball game he experienced violent pain in left Achilles tendon Believed that somebody had kicked him fell down on the floor

Treatment Elastic bandage for 3 weeks plaster for 3 weeks

Subjectively (6 weeks after trauma) Pain in calf on ordinary walking had to walk with tiff foot

Objectively Marked swelling of lower part of leg and ankle Achilles tendon g eatly thickened and tender to palpation both medially and laterally a little further than 10 cm above insertion Depression in tendon contour Dorsal extension in nkle increased to a few degrees more than normal Subtotal rupture? Thomp on s test gave plantar flexion *though with reduced* strength

Preoperative E M G Voluntary activity less than normal mainly medially When medial needle was pushed deeper — into soleus — definite asymmetry was no longer noted Probably partial rupture most likely medially Neurophysiologically complete rupture unlikely as for instance the asymmetry of Hoffmann s reflex seen in complete ruptures was absent

X ray Achilles tendon could not be defined and thus not assessed

Operation (2½ months after trauma) Hardened and greatly thickened peritenon haemorrhag s Underneath the peritenon another layer of hardened tissue at first interpreted as being Achilles tendon Longitudinal incision in this tissue exposed normal tendon tissue and the site of rupture which involved both medial and lateral portion of Achilles tendon 3—4 cm above insertion Soleus portion intact As excision of all devitalized tendon and *granulation tissue left a considerable defect it was necessary to divide* the soleus tendon and let th two parts overlap slightly so as to ensure satisfactory opposition at suturing which thus became step like A minor defect laterally was covered with a flap from the exposed aponeurosis It was considered doubtful whether the final result would be as good as those obtained earlier by operation of Achilles tendon rupture

Histologically Devitalized tendon tissue and highly sclerosed granulation tissue of tendon like appearance *Inflammatory cell infiltration around the* vessels

Outpatient check up (3 months) Seroma or bursa like collection developed in the postoperative course and had to be punctured several times Operation scar normal Otherwise no troubles with Achilles tendon

Return to work 3 months after operation

Postoperative E M G (6½ months) Fully normal

Outpatient check up (1 year and 4 months) *He had been skiing in the win*ter and then trained running without any great discomfort Objectively a fusiform thickening with slight fluctuation was palpated dorsally o er Achilles tendon 2½—9½ cm above insertion Operation scar normal no adhesions No tenderness on palpation over Achilles tendon Atrophy of 1 cm of the calf

Result (1 year and 10 months after operation) Full training no dis omf rt

CASE 14 A 24 year old university student and champion long-distance runner He had had trouble with left Achilles tendon for 1½ years clinically diagnosed as achillotenobursitis Local steroid injection in the calcaneal bursa relieved the symptoms and enabled him to run races until he sustained the injury

Trauma (1½ years before operation) When training barefooted on a golf course he felt a sudden pain in the region of left Achilles tendon immediately above insertion The pain persisted

Treatment Rest Butazolidine ointment After 5 months a steroid injection was given locally at the calcaneal insertion and after another 2½ months into the region of the bursa As no response was noted dimethyl sulphoxide (DMSO) was tried

Subjectively (1 month before operation) Pain and tenderness on increased activity Almost unable to run 50 metres to catch a bus

Objectively Achilles tendon distinctly thicker immediately above insertion and tender to palpation laterally Atrophy of just over 1 cm of triceps surae

Preoperative EMG Volitional activity reduced laterally

X-ray Left Achilles tendon twice as thick as right one

Operation (1½ years after trauma) Achilles tendon looked normal on the whole but 3—4 cm above insertion there was a slightly uneven and raised section Incision revealed a cystic cavity with two rupture ends and profuse granulation tissue and fibrin End to end suture

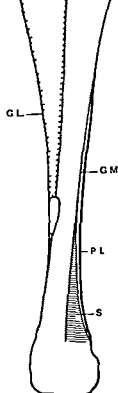
Histologically Devitalized tendon tissue partly transformed into and infiltrated by unspecific granulation tissue with newly formed tendon like connective tissue Some areas were coated with a fibrin like mass

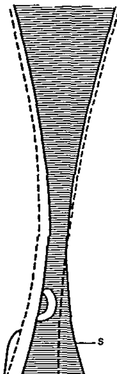
Return to work 10 days after operation

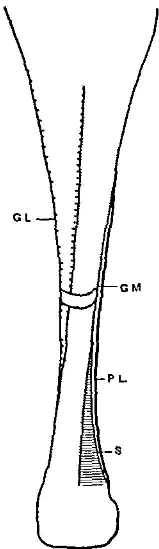
Outpatient check up (3 months) Subjectively no complaints Operation scar normal Full range of movement in talocrural joint

Postoperative EMG (3½ months) Normal

Result (2 years) No troubles with Achilles tendon Training twice a week running 7—8 km He had not resumed competitive sports because of studies among other reasons







CASE 13 A 38 year old engineer and handball player

Trauma During a handball game he experienced violent pain in left Achilles tendon Believed that somebody had kicked him fell down on the floor

Treatment Elastic bandage for 3 weeks plaster for 3 weeks

Subjectively (6 weeks after trauma) Pain in calf on ordinary walking had to walk with stiff foot

Objectively Marked swelling of lower part of leg and ankle Achilles tendon greatly thickened and tender to palpation both medially and laterally a little further than 10 cm above insertion Depression in tendon contour Dorsal extension in ankle increased to a few degrees more than normal Subtotal *rupture? Thompson's test gave plantar flexion* though with reduced strength

Preoperative E M G Voluntary activity less than normal mainly medially When medial needle was pushed deeper — into soleus — definite asymmetry was no longer noted Probably partial rupture most likely medially *Neurophysiologically* complete rupture *unlikely* as for instance the asymmetry of Hoffmann's reflex seen in complete ruptures was absent

X ray Achilles tendon could not be defined and thus not assessed

Operation (2½ months after trauma) Hardened and greatly thickened peritenon haemorrhages Underneath the peritenon another layer of hardened tissue at first interpreted as being Achilles tendon Longitudinal incision in this tissue exposed normal tendon tissue and the site of rupture which involved both medial and lateral portion of Achilles tendon 3—4 cm above insertion Soleus portion intact As excision of all devitalized tendon and granulation tissue left a considerable defect it was necessary to divide the soleus tendon and let the two parts overlap slightly so as to ensure satisfactory opposition at suturing which thus became step like A minor defect laterally was covered with a flap from the exposed aponeurosis It was considered doubtful whether the final result would be as good as those obtained earlier by operation of Achilles tendon rupture

Histologically Devitalized tendon tissue and highly sclerosed granulation tissue of tendon like appearance Inflammatory cell infiltration around the vessels

Outpatient check up (3 months) Seroma or bursa like collection developed in the postoperative course and had to be punctured several times Operation scar normal Otherwise no troubles with Achilles tendon

Return to work 3 months after operation

Postoperative E M G (6½ *months*) *Fully normal*

Outpatient check up (1 year and 4 months) He had been skiing in the winter and then trained running without any great discomfort Objectively a fusiform thickening with slight fluctuation was palpated dorsally over Achilles tendon 7½—9½ cm above insertion Operation scar normal no adhesions *No tenderness on palpation* over Achilles tendon Atrophy of 1 cm of the calf

Result (1 year and 10 months after operation) Full training no discomfort

CASE 16 A 63 year old foreman and gymnast

Fi st trauma During gymnastic exercise practice he felt a snap in right Ach lles tendon, after which the tendon was painful on movement and tender

T e tment Local steroid injection on five occasions as from 10th day after trauma

Second trauma (2 months after first one) On running out of the way of a car he felt as though someone had kicked him on the calf 15 cm above insertion of Achilles tendon

Subjectively Pain on mo ement swelling of tendon A feeling of weakness on plantar flex on of foot

Objectively Defect in medial contour of tendon 7 cm above insertion Tendon felt thinner than normal on palpation Atrophy and reduced tone of med al gastrocnemius belly Dorsal extens on in talocrural joint increased to 5—10 more than normal

P eoperative E M G Volitional act vity much less med ally than laterally

X ray Infiltration of the fat at lower portion of tendon probably due to partial rupture

Ope tion (3½ months after first trauma) Transverse rupture of medial portion of tendon about 7 cm abo e insertion a layer of hardened tissue found o er the s te End to end suture

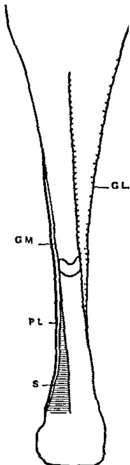
H stolog cally Partially de italized tendon tissue showing transformation into *sclerosed granulat on tissue whi h in parts resembl d t ndon tissue Here* and there lymphomonocytic cell infiltrat on

Retu n to u ork 3 months after operation

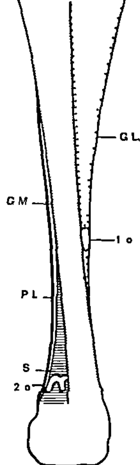
Postope ative E M G (3½ months) Volitional activity symmetric Normal contraction time Hoffmann s reflexes normal

Outpatient check up (1 year and 2 months) Achilles tendon st ll slightly stiff but otherwise no discomfort Operat on scar normal Normal strength in foot and calf muscles though still suggested atrophy of gastrocnemius bellies but normal tone Range of movement in right talocrural joint same as in left one

Result (2 years) Subjecti ely no trouble with Achilles tendon Taking daily walks *skiing 10 km or so without any dis omfort*



6



CASE 15 A 22 year old buyer and champion hurdler with a 1 month history of tendinitis of right Achilles tendon the condition was relieved by rest

Trauma (10 months before operation) During a cross country run he trod on a stone with accompanying hyperextension of right ankle Felt as if something had been torn in the Achilles tendon

Treatment Relative rest for just over 3 months DMSO was tried but produced no effect

E M G (3 months after trauma) Slight reduction of volitional activity Tendon probably not ruptured One local steroid injection cleared the condition for 3 months but the sharp pain returned on increased weight bearing Complete rest for a further 2 months

Subjectively (10 months after trauma) Pain and tenderness over Achilles tendon on exertion and stepping side ways on the foot No discomfort at work

Objectively Right Achilles tendon increased in width fusiform thickening and tenderness on palpation laterally about 5 cm above insertion Atrophy of lateral gastrocnemius belly Dorsal extension in talocrural joint increased to 5—10 *more than normal*

Preoperative E M G Asymmetry of volitional activity which was reduced laterally prolonged contraction time and altered shape of contraction curve *Minor lateral rupture*

X ray Right Achilles tendon much thicker than normal above insertion Oedema in front of insertion

Operation (10 months after trauma) Rupture of the whole soleus portion and small part of lateral portion of tendon about 1 cm above insertion End to end suture after mobilization and shortening of unruptured part of tendon

Histologically Old devitalized tendon tissue and sclerosed granulation tissue resembling normal tendon tissue but having more irregular collagen structure Moderate lymphomonocytic cell infiltration around the vessels

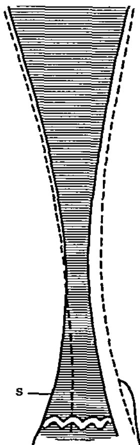
Return to work 3 weeks after operation wearing walking plaster

Outpatient check up (13 months) No trouble with Achilles tendon at sprint rushes badminton and physical exercises Able to run distances of 5 km for 2—3 consecutive days without any discomfort but after that time *Achilles tendon increasingly tender*

Objectively Operation scar normal Tendon contour *slightly irregular Slight* tenderness on palpation immediately above insertion No measurable muscle atrophy

Postoperative E M G Normal

Result (2 years) No trouble at all with Achilles tendon No tenderness after long distance running



CASE 18 A 27 year old farmer and Swedish champion in 10 000 metres

Trauma (5 days before operation) At the end of a 10 000 metre race in an international competition at a height of 2000 metres in Turkey possibly stepping sideways on the raised edge of the track he felt sharp stabbing pain in left Achilles tendon and fell down on the track

Objectively (within a minute of trauma) Distinct tenderness on palpation medially over Achilles tendon maximal tenderness at calcaneal insertion and junction between soleus muscle and free portion of tendon

Preoperative E M G Reduced volitional activity in medial gastrocnemius belly Asymmetry still more marked when the needle was pushed deeper Hoffmann s reflex slightly increased

Operation (5 days after trauma) Haemorrhages beneath peritenon Medial rupture 5—6 cm above insertion involving about ¼ of the cross section of the medial portion of tendon at the border of the soleus muscle Resection of ruptured ends of tendon and suture with grafting plantaris-longus tendon in the resulting tendon defect

Histologically Devitalized tendon tissue with altered collagen stainability and non stainable endoplasm areas Virtually no granulation tissue Slight fibrin exudation

Return to work 3 months after operation

Outpatient check up (7½ months after operation) Resumed training barely 3 months after operation running 8 km 4—5 times a week, occasionally 17 km The main reason for his visit was pain on lateral aspect of left knee *Diagnosis* Tenobursitis No trouble at all with Achilles tendon operation scar normal On palpation Achilles tendon felt slightly thickened over the part into which plantaris tendon was grafted No tenderness on palpation Atrophy of calf over 1 cm but muscle tone normal Normal range of movement in ankle joint

Postoperative E M G Fully normal

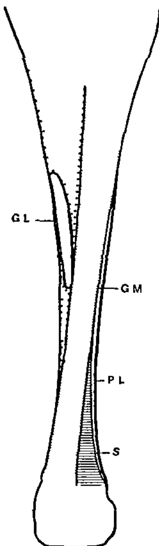
Result (1 year and 7 months) Completed racing season 1 year after operation without any discomfort Still among topperformers running 10000 metres in 30 minutes and 20 seconds in a competition for the Swedish Championship although he did not win it No trouble at all with Achilles tendon

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CASE 17 A 47 year old engineer and allround athlete

Trauma (10 years before operation) After betting he went untrained for a 1500 metre run and felt intense pain in left Achilles tendon Since then he had two — three spells of recurring trouble every year in the form of tingling pain

Treatment Rest during the most troublesome periods otherwise no special treatment no steroids

Subjectively (2 months before operation) After skiing without sustaining any particular injury he noticed swelling in the region of Achilles tendon and had pain even at rest stiffness in the morning

Objectively Left Achilles tendon much broader and thicker than normal tendon contour bulged dorsally just above insertion extending proximally as far as 5 cm below gastrocnemius Tenderness on palpation most marked laterally

Preoperative E M G Distinct decrease of volitional activity laterally

X ray Left Achilles tendon markedly thickened Soft tissues infiltrated

Operation (10 years after the suspected trauma) Several yellow soft areas of granulation tissue interspersed with tendon like hardened tissue Diffuse ill defined infiltration Excision of the soft granulation areas and the hardened tendon like tissue revealed a section extending obliquely laterally *medially suspected to represent the original site of rupture Side to side* suture Diameter of Achilles tendon shortened by just over one third It was considered doubtful whether normal postoperative tendon function would be achieved

Histologically Partial devitalization with hyalinization of collagen and fraying of fibrin structure Profuse formation of fresh and old granulation tissue showing also myxomatous degeneration Foreign body reaction seen in the e areas Sparse unspecific inflammatory cell infiltration

Return to work 4 weeks after operation

Outpatient check up (6 weeks) Operation scar normal Foot easily raised to mid position No tenderness on palpation

Postoperative E M G (1 ½years) Normal

Result (1 year and 7 months) No trouble at all with Achilles tendon 100 % recovery Full training for last 10 months running distances of 7—8 km without discomfort

CASE 20 A 43 year-old bank official and orienteerer with a history of t n dinitis of left Achilles tendon for 10 months no known injury Had to give up racing

Treatment Rest Butazolidine ointment no steroid injection

Subject rely Pain in left Achilles tendon on mo ement Unable to run for more than ½ hour Tendon painful even on quick walking Discomfort in the morning

Objectively Achilles tendon slightly increased in width Distinct tenderness on palpation 3—4 cm above insertion, most markedly laterally Atrophy of calf over 1 cm

Preoperative E M G Volitional activity reduced laterally

X ay Left Achilles tendon slightly thicker in upper part

Oper t on A section of tendon laterally 5—6 cm above insertion, slightly thicker and softer than normal Long tudinal incision At a depth of 3—4 mm an oedematous area in which two normal tendon streaks d sappeared into tissue of opaque appearance — granulation tissue Excision side to-s de suture

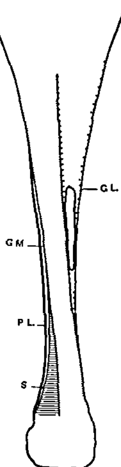
Histologically Devital zed tendon tissue and mostly newly formed granula tion tissue with finely streaked wavy collagen structure not resembling normal tendon tissue Some areas of inflammatory infiltration peri ascularly

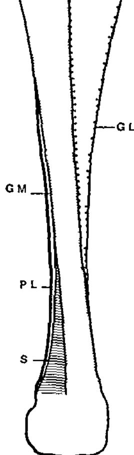
Return to wo k 2 months after operation

Postoperati e E M G (5 months) Volitional activity increased but still sl ghtly less than normal, not asymmetric Furth r regr ssion

Outp tient check up (5 months) Tenderness o er Achilles tendon persisted longer than usual Commenced training but suffered some pain on the following day Operat on scar normal

Result (1 year and 6 months) No trouble at all with Achilles tendon Went for orienteering runs every Sunday and on skis without discomfort





CASE 19 A 28 year old engineer and cross country runner who had a history of tendinitis of right Achilles tendon for 2 years After local steroid injections he was symptom free for 7 and 3 months respectively until he sustained the injury

Trauma (1 year before operation) *During a cross country run he tripped* over root of tree placing excessive weight on right Achilles tendon and felt sharp pain in tendon

Treatment Rest DMSO and one local steroid injection produced no effect Partial rupture suspected

E M G (2 months after trauma) No abnormalities

E M G (5 months after trauma) No abnormalities

Subjectively (9 months after trauma) Had to give up training tried skiing but tendon too painful Complained of pain on ordinary walking and walking up and down stairs

Objectively Thickening and possibly slight irregularity of tendon contour distinct tenderness on palpation 3 cm above insertion of tendon most marked medially Reduced tone laterally atrophy of calf over 1 cm

Preoperative E M C Reduced voluntary activity in soleus and Hoffmann s reflex heightened (150 % of that on left side) central rupture

X ray Right Achilles tendon thickened and poorly outlined soft tissue infiltration Minor areas of calcification in anterior part of tendon

Operation (1 year after trauma) Achilles tendon looked intact but on palpation thickened at the level of lowermost part of soleus Incision revealed central rupture with sanguinolent fluid haemorrhages and several rupture ends *with areas of calcification?* Excision *side to side suture*

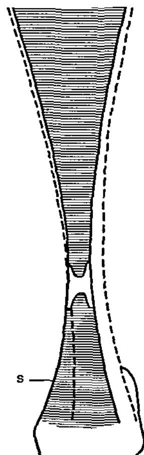
Histologically Devitalized tendon tissue with obliterated fibrous structure poorly stainable endoplasm and altered collagen stainability Tendon *like* granulation tissue partly with marked inflammatory changes

Return to work 6 weeks after operation

Outpatient check up (2 months) Subjectively relatively little discomfort walked without difficulty Operation scar normal No tenderness on palpation Triceps surae function normal *Able to rise on his toes*

Postoperative E M G (3 months) Symmetric and normal volitional activity Hoffmann s reflex and contraction time normal

Result (1 year and 5 months) Commenced training 3 months after operation As he lives in Africa no final check up has been made but according *to information the condition has l a ed up completely*



CASE ? A ? year-old student of technology and international sprinter who had had tendinitis of right Achilles tendon 4½ months before the operation After local steroid injection he had been completely free from symptoms during a period of hard training

Trauma (3½ months before operation) On making a vigorous push off at the start of a 100 metre race he felt an intense jarring pain in the right Achilles tendon No discomfort in daily life but avoided rising on his toes Training impossible

Objectively Irregular tendon contour medially Muscle atrophy and reduced tone in medial gastrocnemius belly Increased dorsal extension in ankle joint

X ray Slightly thickened tendon with oedema towards the fatty space

E M G Reduced voluntary activity medially

Operation Medially two rounded-off rupture ends enclosed by granulation tissue Plastic repair using the plantaris longus tendon

Histologically Devitalized tendon tissue with a few necrotic areas (suggested calcification) Tophus like sparse granulation tissue

Return to work 1 week

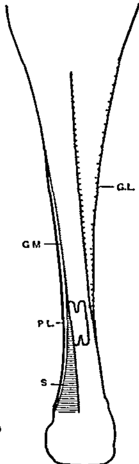
Postoperative E.M G (3 months) Normal

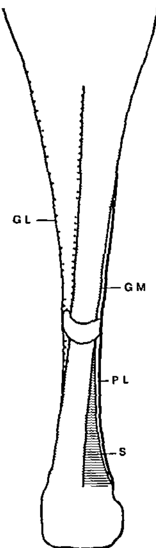
Postoperative E M G (8 months) Normal

Outpatient check up (8 months) Gradually increased training Able to do high jumping of 1 8 metres but some diffuse pain on sprint training

Outpatient check up (13 months) Probably started too hard training in interval as well as long distance running had developed diffuse pain further laterally which gave rise to suspicion of imminent lateral rupture Operation scar normal but Achilles tendon felt slightly indurated and had not resumed its normal soft elastic consistence E M G was still wholly normal

Result (15 months) He had completed another period of hard training and was free of all symptoms Training 3—4 days a week long-distance running over 8—9 km and interval running over 6 times 1000 metres or 300 metres at relatively high tempo No trouble at all with Achilles tendon





CASE 21 A 45 year old *taxi driver and amateur athlete* who for 7 months had had trouble with his left Achilles tendon following a road race After local steroid injection on two occasions he had no trouble for 2 months until the injury occurred

First trauma (3½ months before operation) On kicking a ball he felt a snap in his left calf medially Partial rupture was suspected but E M G showed no definite abnormalities

Second trauma (2 days before operation) During a 400 metre run he felt violent sharp pain and an audible snapping in the region of left Achilles tendon He completed the race and was then admitted to Serafimerlasarettet

Objectively Transverse indentation in tendon contour and marked tenderness on palpation over *tendon 3—4 cm above insertion Haematoma Thompson's* test gave normal plantar flexion but with slightly reduced strength

Preoperative E M G Volitional activity greatly reduced in lateral and medial *gastrocnemius bellies No definite asymmetry No difference in con* traction time between the two legs but downward deflection of curve markedly prolonged on left side

Conclusion Partial rupture *soleus portion should be intact*

X ray Achilles tendon thickened locally its anterior portion poorly outlined against the fatty space

Operation (2 days after trauma) Bleeding under peritenon towards gastrocnemius bellies Transverse rupture through medial and lateral parts of tendon 4—5 cm above insertion but soleus portion intact End to end suture The soleus tendon which was too long after resection of the two rupture ends was sutured both to the medial and to the lateral side of *the already sutured rupture ends*

Histologically Streaks of devitalized tendon tissue Sclerosed tendon like granulation tissue predominated Both old and fresh haemorrhages Sparse fresh granulation tissue *around haemorrhages and vessels Minimal in* flammatory cell infiltration

Return to work 2 months after operation

Postoperative E M G (4 months) Normal

Outpatient check up (9 months) No complaints whatsoever Trained and competed in track and field athletics without any trouble with Achilles tendon Had noticed slight thickening of tendon contour about 10 cm above insertion but no tenderness on palpation peritenon possibly slightly thick*ened in this area* Operation scar normal

Result (1 year and 3 months) No complaints Recommenced full training and competing

CASE 4 A 19 year old office clerk and med um dista. ce runner

Traums (8 months before operation) On running indoors on a hard wooden floor he felt sharp pain in right Achilles tendon

Treatment After steroid injection medially at insertion of tendon the tenderness over this area disappeared The troubles returned when he commenced trai ng

Subject vely Stabbing pain in Achilles tendon on attempts at training and on walking up and down a flight of stairs

Objectively Slight swelling of peritenon, fairly intensive tenderness on palpation from insertion of tendon for just over 6 cm in proximal direction Uncertain whether pain was localised more laterally or more medially On palpation of relaxed tendon the point of maximal tenderness was laterally 6—7 cm above insertion Slight atrophy of lateral gastrocnemius belly

P ope ative E M G (on two occasions) Some decrease of volitional activity in lateral gastrocnemius belly Hoffmann s reflex heightened Shortened contraction time deformed contraction curve

X ay Right Achilles tendon somewhat thickened

Ope ation Dorsally Achilles tendon normal Ventrally indurated section at junction between soleus muscle and lateral portion of tendon Removal of granulat on tissue revealed a rupture of ventral portion of tendon 5 cm in length and extending slightly obliquely End to-end (side to side) suture

Hi tologically Partially devital zed tendon tissue with altered collagen stain ab lity and poor stai iability in endoplasm areas Narrow streaks of newly formed granulaton tissue r ch in collagen and of tendon like structure Very sparse monocytic inf ltration around some small vessels

R tu n to work 7 weeks

Po tope tive E M G (3 months) Normal Only slight asymm try of volitional acti ity medially laterally

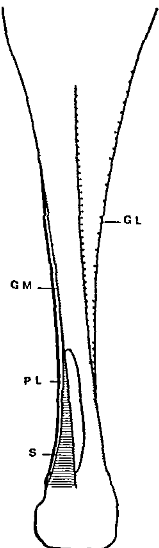
Outpatient check up (3 months) No trouble with Ach lles tendon, apart from sensation of cramp in calf muscles on riding a bicycle ergometer Operation scar normal No tenderness on palpat on Gradually increased tra ning

Result (1 year and 1 month) Able to run maximum 20 km without any tro ble with Achilles tendon for the first 8—9 months after oper tion Then he fell ill w th pleurisy Strength of leg and tendon returned after disk bar tra ning

S

P L.

G L



CASE 23 A 23 year old gymnastics master and medium distance runner with a 7 month history of tendinitis of right Achilles tendon at insertion laterally After local steroid injection he was symptom free for 3 months

Trauma (3 months before operation) Sharp pain medially in Achilles tendon after training Persistent pricking pain probably due to pressure of shoe stiffener while running in training shoes with built up heels

E M G No abnormalties

Treatment Rest from training

Subjectively (1 month before operation) On attempts at training he suffered pain sometimes so sharp that he could hardly walk

Objectively Tendon contour irregular medially a few cm above insertion tenderness on palpation over this area

Preoperative E M G Volitional activity reduced medially Medial rupture suspected

X ray Dorsal border of fatty space in front of Achilles tendon somewhat indistinctly outlined

Operation A thick tendon like thread extended medially from Achilles tendon a good 5 cm above insertion obliquely into the thickened wall of the bursa to which it adhered Partial medial longitudinal rupture Excision side to side suture

Histologically Coarse bundled connective tissue rich in collagen only slightly resembling devitalized tendon tissue and granulation tissue highly sclerosed and tranformed into tendon like tissue

Return to work 6 weeks

Outpatient check up (7 months) Unable to commence training for the first few postoperative months but had cycled instead Laterally above insertion slight thickening which was tender to palpation — peritenon? It had virtually disappeared at the time of examination Lately he had trained at irregular intervals Operation scar normal

Result (13 months) Training 4 times a week running 10—15 km No trouble with the right Achilles tendon but some discomfort from the left one

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RAGNAR KALÉN

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From the Department of Orthopaedic Surgery
University of Gothenburg Sweden
(Head Professor Carl Hirsch)

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MUNKSGAARD COPENHAGEN 1968

From the Swedish by Lois Goldie Carlson

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Contents

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Introduction

At the end of last century arthrodesis was introduced as an operative technique for various disabilities and lesions of the hip Since then how ever the attitude towards and the indications for this method have varied It is now accepted in orthopaedic surgery and has become one of the classical treatments Many problems are involved in the use of this tech nique and therefore extensive research work especially clinical has been carried out

The operation is of a major kind and for a long time implicated pri mary mortality at a rate which could not be disregarded The improved technique of anaesthesia and the control of fluid balance have almost elimi nated these risks Longstanding immobilization is necessary to achieve fusion This results in a high frequency of post operative complications such as thromboses embolism stiffness of the knee joint respiratory and urinary tract infections and so on To shorten the time of immobilization numerous methods of internal fixation have been suggested The aim has been to make the primary fixation of the joint components stable enough to allow the patient to get out of bed early and also to avoid plaster immobilization of other joints

The proposed methods of osteosynthesis have been elaborated clinically The efficiency of these methods have been reported as part of all the fac tors which are involved in the clinical healing results

In this study an attempt is made to explain theoretically and experi mentally the conditions of osteosynthesis in arthrodesis of the hip Further more experiments were carried out to establish the effectiveness of different methods in achieving primary stability For this purpose a suitable tech nique was elaborated

PART I

Historical Review

The surgical procedure *arthrodesis* carried out to prevent mobility of a joint by fusion, was denominated by Eduard Albert in 1877 In 1878 he performed this operation in a knee joint and in 1892 in a hip joint At that time however several other authors had described the operation in the hip Heusner (1884) and Lampugnani (1885) had performed operations on a few cases of congenital dislocation Lagrange (1886) Dollinger (1891) and Daraignez (1891) described operative techniques using different kinds of internal fixation In 1892 von Winiwater also applied arthrodesis of the hip

Besides Alber Albee contributed at an early stage by introducing arthrodesis of the hip His first case reported in 1908 was very successful The indication was osteoarthritis and the arthrodesis was performed by using an intra articular technique adductortenotomy and fixation with a larger plaster hip spica Five weeks later the plas er was removed up above the knee and after nine weeks the patient was mobilized After four months he was back working as a patrol man

An important indication at this time was the various types of infection in the hip especially tuberculous arthritis The aim was if possible to avoid engaging the actual joint in the operation In 1913 Maragliano and Albee performed the first extra articular arthrodeses with bone grafting The graft was applied in an ilio femoral position Various positions of the graft were described during the 1920 s by a number of surgeons Maragliano (1919) described a technique of ischio-femoral bone grafting as well as Trumble (1931) Brittain (1932) developed this technique to the so called ilio femoral V arthrodesis

During the 1930 s attention was again directed to a combination of the different techniques of arthrodesis with internal fixation

Van Nes (1932) Burns (1935 1939) and Watson Jones (1934 1938) emphasized the importance of stable immobilization to obtain a successful result The immobilization was not considered satisfactory unless internal fixation completed the plaster spica The technique of osteosynthesis re

Besides the general complications as a consequence of the operation the difficulty is associated with ensuring successful union In so-called fibrous healing some authors have reported good clinical results (Charnley 1953 Mortens 1960 Morris 1966) As opposed to bone union pain was however not always abolished Die Arthrodese kann natürlich nur zur Schmerzfreiheit fuhren wenn eine vollkommene ossare Ankylos eintritt (Schindler 1958)

The high frequency of non union as reported by some authors (inter alia Stinchfield Cavallaro 1950 Cholmeley 1956 Lipscomb and Mac Caslin 1961 Williams 1962) accounts for the hesitation in adopting this technique

Attempts have been made to improve the union by large and well fitting contact surfaces bone grafting by improved methods of fixation, subtrochanteric osteotomy and longstanding immobilization in plaster

The surgeon s aim is to bring about a union in the best functional position with the shortest possible bedrest

Important factors of the operative technique are

I Position of Arthrodesis
II Contact Surfaces and Bone Grafting
III Technique of Internal Fixation
IV Subtrochanteric Osteotomy in Arthrodesis

commended by these authors, and gradually coming into usage was fixation with a three-flanged nail

Some methods elaborated during the last decades include derangement of the joint This was done by resection of the caput, dislocation of the caput through the acetabulum (either by fracturing the acetabulum or reshaping the caput and dislocating it into a bore in the acetabulum) or by pelvic osteotomy with dislocation (Charnley, 1953 Kuntscher, 1953, 1956, Muller, 1953, Dwyer, 1961)

Arthrodesis was during the last two to three decades challenged by competitive methods, such as different types of arthroplasty and osteotomy At the end of the 1930 s it was believed that one plastic operation was carried out in ten arthrodesis, while twenty years later plastic operations and arthrodesis were performed in a ratio of two to one (Friberg, 1958) At present the reverse seems to prevail as compared to the 1930 s Many authors advocate the great advantages of arthrodesis Albee (1921) thus writes 'There *is hardly any operation that gives a larger percentage of very grateful and satisfied patients than the arthrodesis* Watson Jones (1956) maintains 'No operation is more advantageous to the patient, more satisfactory to the surgeon, more reliable for restoration of the function Blount (1956) says Arthrodesis of the hip is one of the *most valuable procedures for the relief of disease pain or disability of the* hip Crawford-Adams (1966) points out the advantages of arthrodesis Its reliability in abolishing pain, the stability it affords, its capacity to stand up to hard work and its permanence Hobler (1964) believes Die Arthrodese schafft ein stabiles Bein fuhrt zu Schmerzfreiheit burgt fur ein relativ gutes Gangbild und ist unabhangig vom Muskel gleichgewicht He also quotes Creyssels 'Bedauert man manchmal eine Arthroplastik gemacht zu haben so bedauert man selten den Endschluss zur Arthrodese gefasst zu haben

The main disadvantage of arthrodesis of the hip is the actual object of the operation namely the loss of mobility in the joint The motor function of the body changes, the gait may be affected and it may be difficult to carry out certain movements especially the lumbar spine will be subjected to further tension If ankylosis can be achieved in a functional position which is the most suitable for the individual the restrictions will be reduced It is also noteworthy that the indications for the operation are generally based upon severely restricted movements of the joint connected with pain The pain is often associated with muscular contractures which are believed to result also in restricted lumbar mobility With abolishing pain the patient often gets a paradoxical sensation of a greater range of movement

TABLE I

Author	Year	Degree of Flexion	Degree of Abduction	Degree of outward Rotation
Albee F H	1908	10	10	0
Watson Jones R	1938	25–30	0	0
Bailey E.T				
Jackson Burrows	1939	30	0	0
Burns B H	*1939*	*25*	*0*	*0–5*
Girdlestone G R	1940	10 years 10 15 years 15 20 years 25 adults 30–35		
Karlen A	1944	25	0	0
Niebauer J				
King D	1946	35–50	0	—
Smith A de F et al	1949	25	—	—
Steinchfeld & Cavallaro	1950	35	10	15
Merle d Aubigne R	1952	30	—	—
	1965	20	0	0
Mayr H	1953	25	0	0
Charnley J	1953	10 Women 30	0	0
Ehalt W	1954	20	0	5
Stone M M	1956	30	10	15
Lindstrom N	1956	20–30	0	0–5
Blount, W P	1956	30	0	0–5
Thompson F R	1956	20	– 5	0
Watson Jones R				
Robinson W C	1956	30	Max 15	0
Lancotti G	1958	20–25	0	0
Hibbert J	1960	25	–10	5
Sicard A & Gerhard J	1960	20–25	5–10	0
Cozzolino A	1960	20–25	0	0–5
Lipscomb P R				
McCaslin F E	1961	15–20	0	0–5
Neely D C	1961	20	10–15	0
Konforti B	1962	5–10	0	0
De Palma et al	1962	20	0	0
Alk I	1962	25	–2 – –5	0–5
May V R & Mauck W	1962	15–25	10–15	0
Graham E C	1963	*10–15*	5	5
Tok G S et al	1964	Max 20 (25–30 in person walking in a sitting position)	0	0
Verhaugen & Navarre	1964	Max 30	0	5–10
Hibler W	1964	25	0–8	10–15
Lenoble J-C	1965	20	0	0
Ga h x, J et al	1965	10–20	0	0
Crawford Adams J	1966	15–20	0	0
Lindahl O	1966	45 (angle of flexion measured from the maximum extension of the healthy leg)	0	0–5
[illegible]	nd	40	10–15	10–15

I Position of Arthrodesis

In the literature published during the last three decades, the authors seem to agree upon the recommended positions The usually recommended position is flexion at 20—30 degrees, neutral position between abduction and adduction, and outward rotation at 0—10 degrees (Table I) The lack of a well defined initial position from which the angles are measured is remarkable however

Usually, the desired flexion is achieved by using the technique recommended by Burns and Watson-Jones The patient is lying on his back with his leg in contact with the table The lordosis of the lumbar spine is then supposed to correspond to a flexion in the hip of 20—30 degrees Lindahl (1966) measured the angle between the normal leg at maximum extension and the leg to be arthrodesed The angle between the legs should then be about 45 degrees Together with Ahlback (1966) Lindahl also described a roentgenological measuring technique

In the frontal plane the position should be neutral Abduction is recommended when leg shortening has to be compensated Lindstrom (1956) however warned against compensating shortening through abduction as the gait will deteriorate Konforti (1962) claimed that an abduction position will cause increased back pain

Several authors point out the difficulty in measuring the angle for abduction/adduction Furthermore, the neutral position gives an angle between the longitudinal axis of the femur and the vertical plane at 5—10 degrees in a standing position (Weinreich 1959 Herbert 1960 Crawford Adams 1966)

Adams (1931) adopted Kingsley s and Lovett s methods from 1888 for measuring flexion and abduction Dickson (1951) designed a so called coxometer in order to facilitate angle measuring in both the sagittal and the frontal planes Lindahl (1965) introduced a technique for determining the abduction by measuring the distance between the medial malleoli with the legs together A difference of 1 cm means an abduction of approximately 3 degrees

The adduction position ought to be avoided due to the risk of disturbed balance and gait Herbert (1960) however stated that an adduction of 10 degrees would be suitable and Alvik (1962) suggests 2—5 degrees The

II Contact Surfaces and Bone Grafting

1 Intra articular Contact

The first arthrodeses were performed as intra articular procedures Albee (1908) used a chisel to plane the upper part of the caput so that this would fit against an equally planed acetabulum By dislocation of the joint and removal of the cartilage from the joint surfaces attempts were made to improve the contact surfaces Watson Jones (1938) recommends this technique combined with internal fixation Attitudes towards dislocation of the joint vary The critics especially Charnley (1953) maintain that the contact surface actually becomes smaller by the caput being reduced relative to the acetablum According to his technique the caput/collum are converted into a cylindrical or cone-shaped plug which will fit in a drilled bore through the acetabulum into the pelvis Dickson (1947) tries to avoid reducing the caput in relation to the acetabulum by laminating the cartilage so that the surfaces will remain congruous Another method is to adjust the cavity in the acetabulum according to the size of the caput by using a suitable milling tool Smith and Baab (1949) recommended dislocation in order to remove the cartilage entirely At the same time they drilled several bores in the caput to facilitate the healing Vogl (1950) described a method where the caput is not dislocated Instead he used a chisel through the collum/caput chipping the joint surfaces Schindler (1958) dislocated the caput and inserted an ilio femoral bone graft A similar procedure is recommended by Tsoukas (1964)

The advantage of completely removing the articular cartilage is that a large bone contact is obtained The disadvantage is that the operation will be more extensive that the nutrition of the caput will be jeopardized by the dislocation and that the position of the joint adjusted prior to operation may not be maintained Lange (1958) believed that dislocation of the caput will not improve healing but instead increase the risk of non union Lindstrom (1956) Hobler (1964) and Chapchal (1965) amongst others do not believe in a better result if the joint is dislocated The operation becomes more extensive and the nutrition of the caput will be impaired In connection with internal fixation Chapchal also believes that the ligament and the capsule will offer resistance when the nail is hammered into the acetabulum Verheugen & Navarre (1964) reported non union in 10 per

initial position from which these degrees were measured has not been specified Merle d Aubigne (1963) defined the neutral position thus The line transversing the centre of the femoral head and the centre of the medial condyle of the femur should be perpendicular to the line through the acetabulae He believed that a slight adduction will not cause any disturbance while abduction causes limping compensatory scoliosis and back pain

For the rotation, zero position or slight outward rotation is recom mended Charnley (1953) warned against inward rotation as it will then be impossible to take a normal step

In order to get a suitable position from the point of rotation, it is re commended that the patella should be directed upwards when the patient lies on the operating table

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cent of their cases of intraarticular arthrodesis with luxation of the joint and 15 per cent without dislocation

2 Bone Grafting

Since Marigliano and Albee in 1913 performed their first cases of bone grafting, the development of this technique became of current interest The use of bone grafting was to obtain a bridge between the pelvis and the femur, to stimulate the bone regeneration and achieve stabilization The bone grafting also enabled bridged healing without engaging the actual joint This was considered advantageous when infections occurred in the joint especially tuberculosis, which at that time was a usual indication for arthrodesis of the hip

There are several ways of classifying the methods of grafting The easiest way is to classify according to the positions of the graft, a) the ilio femoral and b) the ischio femoral bone grafting

a) *Ilio-femoral Bone Grafting*

The ilio-femoral bone graft can be placed in an extra articular, a para-articular or an intra articular position The extra articular technique is re commended by Albee (1919), Hibbs (1926) Key (1926) Wilson (1927), Schumm (1929), Girard (1935) Para articular bone grafting has been described by Nove-Josserand (1921) Hass (1922), Mathieu (1926) Albee (1929), Sorell (1930) Henderson (1933) Harris (1935) Kellog Speed (1937), amongst others

This procedure has also aroused much interest amongst several authors during latter decades Thus Davis (1954) used a crista graft with the muscular insertion intact, to ensure blood supply The graft is placed in a groove across the joint after removal of the articular cartilage Decoulx (1965) modified this technique He did not dislocate the joint and performed subtrochanteric osteotomy Cattaneo (1959) used a graft from the greater trochanter and displaced it into the ilium completing with a trans articular graft from the tibia His experimental investigations revealed that the tibial graft is the strongest the femoral on the other hand is superior to a graft from the fibula

Schindler (1958) described a technique resembling that of Hibbs After removing the articular cartilage a graft of about 12 cm is taken from the lateral side of the greater trochanter and the femoral shaft It is rotated 180 degrees around its upper end and is fixed to the ilium He believed that the graft will offer complete stability Boytchev (1960) drilled a tunnel penetrating the greater trochanter and part of the ilium Through this tunnel he hammered a suitable bone graft taken from the tibia Boos (1963)

chiselled off the upper parts of the greater trochanter and the femoral head superseding these by a processed bone Hens ge (1967) also used a processed bone which is inserted as a 13 mm coarse bar into a drilled bore trans articularly via the neck and the head

The procedure nowadays in general use is to place a graft from the ilium across the upper part of the joint possibly combined with removal of the articular cartilage and internal fixation (Ghormley 1931 Watson Jones 1938 Lange 1951 Lindstrom 1956)

b) *Ischio femoral Bone Grafting*

De Beule (1909) was the first to describe ischio femoral arthrodesis He resected the head and part of the neck and after medial displacement of the femoral end towards the ischium he used a screw for fixation He did not use any graft Maragliano (1919) published an ischio femoral bone grafting technique Trumble (1931) used a graft which was placed in a rectangular opening cut in the posterior subtrochanteric part of the femur and continuing into a cleft made in the ischium Other authors connected with this technique are Galland (1931) Calve (1932) and Gutierrez (1935) As a rule the graft was taken from the tibia or the fibula Kirsch (1939) however used the 10th rib as a graft

Brittain (1942) developed the ischio-femoral technique into his standard method He emphasized that in arthrodesis the leg tended to become adducted during healing due to the strength of the adductors By placing the graft in an ischio femoral position it will be subject to compression as opposed to a graft in an ilio femoral position which will be subject to tension From the mechanical and healing points of view he preferred the ischio femoral position Later he combined the operation with subtrochan teric osteotomy and internal fixation with a nail Through the osteotomy the graft is placed into the ischium The technique has varied with respect to grafting osteotomy and internal fixation Howard (1950) considered that a long period of plaster immobilization was unnecessary and that the patient could walk with crutches after a few weeks time In his series of 17 he reported 14 cases of ankylosis King (1952) stabilized the osteotomy with a plate to avoid plaster Resina (1954) turned the graft 90 degrees on its side His aim was to achieve a greater stability of the osteotomy This does not coincide with Brittain s idea He claimed that the osteotomy should not be fixed but remain unstable to reduce the stress which otherwise would occur in the arthrodesis because of the long lever formed by the femur

Crawford Adams (1966) gave a survey of the results of various ischio femoral procedures In 7 series reported independently totalling 115 cases

cent of their cases of intraarticular arthrodesis with luxation of the joint and 15 per cent without dislocation

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III Techniques of Internal Fixation

Already when the first reports were published on arthrodesis of the hip the authors were aware of the fact that stabilization was of importance for the union The best healing conditions were created by eliminating the movement between the surfaces which were to be joined During the first decades of the 20th century this was attempted by using a full length hip spica At the end of the 19th century different types of internal fixation had been tried however Lagrange (1886) used two carpenter nails Dollinger (1891) described one method with bolt reinforcement and another with a silver thread stretched between a plate on the inside of the pelvis and a plate on the greater trochanter In the same year Roersch and Daraignez independently, suggested fixation by the use of an ivory pin

The great problem was to obtain non corrosive osteosynthetic material at this time This reduced the interest for internal fixation Not until the 1930 s did the question arise again about improving the primary stability by internal fixation

1 Fixation with Three Flanged Nail

Van Nes (1932) used a thin nail for the osteosynthesis He was discontented with the stability and therefore tried two crossed nails Finally he changed over to a three flanged nail of a larger dimension than the usual Smith Petersen nail Watson Jones (1934) pointed out that the bad results with failures up to 50 per cent were caused entirely by inadequate immobilization In a series of 16 cases he had inserted a three-flanged nail through the joint all of which fused He compared this with the fixation in femoral neck fractures and emphasized the importance of counteracting rotation In his report Burns (1938) mentioned that in 1935 he began to use a coarse three flanged nail He agreed that the bad union depended on the inadequate fixation To begin with he used a three flanged nail of 20 mm diameter but experienced that in many cases it split the trochanteric region Consequently he changed over to using a nail of the Watson Jones type with a diameter of 15 mm slightly coarser than the Smith Petersen nail (13 mm)

The three-flanged nail has since predominated This method has been discussed by many authors mainly from the following points of view

operated according to Trumble, there was a mean healing of 81 per cent 11 series including 260 cases, operated according to Brittain without internal fixation, show the same rate of fusion 5 series, 278 cases, operated with V-arthrodesis (ischio femoral graft + nail fixation) fused in 84 per cent In Crawford-Adams opinion the disadvantage with Trumble s and Brittain's methods is the long period of immobilization in plaster On the other hand, Brittain s technique of subtrochanteric osteotomy offers the possibility of correcting a malposition and of eliminating the long lever of the leg Anyhow, there is a risk of pseudarthrosis in the osteotomy Mayer (1948) warned against lesions of the sciatic nerve In his experience it is unadvisable to take the graft from the tibia because of the high rate of post-operative fractures He recommended that the graft instead should be taken from the ilium An additional problem is the limited mobility of the knee joint caused by long-term immobilization in plaster Vesley (1961) kept the plaster on for six months In his series of 44 cases no patient above 20 years of age regained full mobility of the knee-joint

Finally, combinations of ilio femoral and ischio femoral grafting are reported (cf Lapras, 1965) Greenberg (1952) inserted grafts through drilled tunnels into the ischium as well as the ilium and through the joint

normal procedure in arthrodesis of the hip para articular grafting fixation with a three flanged nail followed by immobilization for three or four months The nail should be directed towards the deflection point of the ileo-pectineal line and the tip of the nail penetrate the internal cortex Mayr (1953) stated the same direction in his series of 200 cases Viernstein (1956) held forth that merely a three flanged nail will not offer satisfactory fixation without immobilization in plaster His series included 326 operated cases

Among the authors who during the 1960 s discussed the problem of the position of the nail and its stabilizing ability Herbert (1960) suggested that it ought to be directed backwards upwards through the collum towards the lower part of the sacro iliac joint Sicard & Gerhard (1960) instead placed the nail in the longitudinal axis of the neck if possible slightly backwards Thompson (1961) pointed out that when the nail is placed centrally it will not have a safe grip in the pelvis In order to obtain this it must be directed backwards If at the same time the nail is in the centre of the collum it means that the arthrodesis must be carried out with inward rotation He mentioned that Wright for that reason used a curved Smith Petersen nail Castaing (1962) showed pictures of a centrally positioned nail Graham (1963) tried to direct the nail backwards and penetrated the internal cortex at the ilio pectineal line by a more ventral insertion in the femur Gardiner (1962) prefered a depth in the acetabulum of 2½ cm with the nail through the weight bearing area of the femoral head Kempf et al (1964) attempted a more vertical direction of the nail so as to prevent flexion extension A Bohler nail was used at a depth in the acetabulum of 3—4 cm Tsoukas et al (1964) also employed a Bohler nail They kept their patients immobilized in plaster for three months Cauchoix et al (1965) also advised a coarser nail but later changed over to fixation with two screws Dickson & Hartman (1965) used a technique which on the whole corresponds to that of Watson Jones The patients were mobilized 4—6 weeks after the operation but plaster was not always applied On the other hand the patients must use crutches up to six months The rate of non union in the follow up was bareley 12 per cent

Crawford Adams (1966) inserted the nail about 2 cm below the greater trochanter and directed it towards the centre of the iliac fossa with an inclination forwards at about 15 degrees The tip of the nail will then emerge at the arcuate margin of the pelvis Charnley (1953) and S t Clair Strange (1965) emphasized the anatomical fact that an angle in the transverse plane is formed by the neck of the femur and the body of the ilium This means that the nail in order to reach deeper into the ilium must be inclined backwards

a) Technique (position of nail ability to stabilize, plaster immobilization)
b) Complications

a Technique

Watson-Jones (1938) described the technique he used for arthrodesis of the hip and advised that *the nail should penetrate 2 5 cm* into the acetabular roof and that the immobilization *in plaster should be maintained* for 2½ months In 1956, he stated that the position of the nail should be *oblique in the collum* In his series of *120* cases *94* per cent healed Haggart (1945) reported a series operated according to Watson-Jones tech nique He pointed out that the nail prevents adduction and rotation but not completely, flexion-extension

Burns (1939) indicated an inclined direction of the nail through the collum in the frontal plane He mentioned that roentgenologically, an anterio posterior view will not reveal if the nail is safely secured in the pelvis The tip of the nail may seem to lie in the bone while in reality it lies inside the true pelvis Thompson (1961) also remarked on this pheno menon In order to avoid an erroneous position of the nail, Burns re commended that a special oblique view should be taken as well

Bailey & Jackson Burrows (1939) *advised a steeper direction of the nail* than for fractures of the collum The insertion should be made further down in the femoral shaft, about 1 25 cm behind the anterior surface of the femur *The nail will then perforate the upper area of the caput* The operation includes drilling of several bores through the head to achieve a more rapid union An objection is that the resistance of the caput will be impaired with unsatisfactory securing *of the nail as a result*

Harris (1943) suggested that the nail should be placed along the longi tudinal axis of the collum through the acetabular internal cortex Further more he inserted a trans-articular graft but was not satisfied with the fixation and therefore applied a plaster hip spica He believed that rotation still may be possible and drilled a Kirschner wire through the distal femur with the ends outside the plaster The immobilization in plaster continued for four months A main complication is the limited mo bility of the knee joint which often occurs

Karlen (1944) and Ehalt (1954) were of the opinion that *the nail should* be inserted 4 cm into the pelvis The latter recommended a nail of the Bohler type which is slightly coarser than an ordinary three flanged nail None of the authors discuss how *to reach the desired depth Arriola* (1952) who used a van *Ness nail said that* ohne Zweifel ist die Länge und Dicke des Nagel ein wichtiger Faktor der Fixierung

In his textbook on orthopaedic *surgery* Lange (1951) described the

drilled in the acetabular roof The nail will then be easier to hammer in and the osteogenesis will improve according to the principle of Beck drilling in pseudoarthrosis He also designed a special shape of the three flanged nail Mayr (1953) reported a series of 167 cases of arthrodesis where in four cases the nail could not be hammered in because of a sclerotic acetabulum In one of these the acetabulum fractured

e) The rate of post-operative subtrochanteric fractures is rather high Bailey & Jackson Burrows (1939) suggested that a short hip spica should be kept on for a long period because of the risk of subtrochanteric fractures Lindstrom (1956) had one fracture in 41 cases followed up Chapchal (1962) had two fractures in 91 cases and in another series of 114 there were five subtrochanteric fractures Haw (1964) had three in 30 cases and Merle d Aubigne (1964) had 13 subtrochanteric fractures in his series of 240 cases four of these occurred at the site of the insertion of the three flanged nail This was one reason for his changing over to fixation with screws Ehalt (1954) suggested a nail and plate to avoid the fracture a method which also was supported by Gardiner (1962) and Crawford Adams (1966) Gardiner performed V arthrodesis on his series and had 7 fractures in 54 cases Verheugen & Navarre (1964) reported 70 cases 28 of which were stabilized with double three flanged nails and 42 with a single one The rate of fractures among the first ones was 21 4 per cent and the latter 4 7 per cent The weakening of the proximal femur caused by insertion of the three-flanged nail increases considerably when a parallel nail is introduced in addition

2 Other Methods with Trans Articular Nailing

The technique of osteosynthesis with a trans articular nail has been modified by many surgeons Kuntscher (1953) pointed out that one nail is unsatisfactory as it does not prevent rotation He recommended stabilization with two curved nails In his opinion one nail could possibly suffice provided that it is curved A plaster hip spica is not required instead mobilization can commence after two weeks He suggested furthermore that the caput acetabulum should be drilled in a coneshaped bore in order to avoid stress concentration and refered to Martin s experiments Lechten (1956) operated on 16 cases according to Kuntscher s method On the radiographs only ten revealed union and four slipping of the nail Weiss & Munzenberg (1962) published a critical article with a series of 30 out of which only 4 united Witt (1965) criticized Kuntscher and pointed out that on the pictures demonstrating his technique the nail did not lie in the bone but inside the true pelvis which results in an unsatisfactory securing of the nails

Radulescu (1964) suggested a completely different position He inserted the three flanged nail from behind through the caput into the acetabular portion of the pubic bone He believed that the conventional position will not prevent rotation, on the contrary to his technique The method has been tried on specimens, but no comparative experiments on stability have been carried out The described position means that the nail will penetrate the thin cortical layer of the caput and that the bone available is not fully utilized

b *Complications*

The risks of complications which may arise are
a) fracture at insertion, b) nutritional disturbances c) diastasis of the joint, d) difficulties to insert the nail into the acetabulum e) subtrochanteric post operative fractures

All these complications can be more or less referred to the shape and the size of the nail

a) The risk of splitting the femur at insertion is especially pronounced when using three flanged nails of a coarser dimension For instance, Burns for this reason changed over from a nail which had a diameter of 20 mm to a thinner one It is also essential to prepare the entrance into the femoral cortex carefully which Watson Jones (1956) and Chapchal (1965) amongst others have pointed out When the cortex of the femur is fractured, the securing of the nail will be impaired (Karlen 1944 Nystrom, 1944)

b) Disturbances of the nutrition in connection with osteosynthesis of femoral neck fractures have been mentioned (Compere & Lee 1940 Linton, 1944 Brodetti 1961) Campell (1937) reported that the nail disturbs the nutrition partly through direct vascular lesions, partly by preventing revascularization Furthermore when arthrodesis is contemplated, the nutrition of the caput and the acetabulum is already disturbed in many cases Merle d Aubigne (1964) warned against extensive dissection of the proximal femur as this may result in necrosis of the femoral head

c) Several authors mention that diastasis easily occurs in the joint when the nail is hammered into the acetabulum Generally diastasis is overcome by some blows with the hammer against the greater trochanter after the nail has been put into place (cf Mayr 1953) Lindstrom uses a modified nail extractor with which he compresses the head against the acetabulum Unander Scharin (1965) has described the instrument Crawford Adams applies a screw across the joint parallel and above the guide-wire in order to avoid diastasis

d) Sometimes it may be difficult to hammer the nail into the acetabular roof Karlen (1942) suggested that in these cases several bores should be

not fully utilized to secure the nails and the resistance of the bone will become further impaired by the trauma caused by the drilling

Stinchfield & Cavallaro (1950) had a series of 117 cases in which the mean rate of non union was 23 per cent Of 11 cases stabilized with a three flanged nail combined with intra juxta articular arthrodesis all but one united Of 10 patients on which fixation was carried out by using three thin Vitallium nails in different directions all united

3 Screw Reinforcement

Osteosynthesis with screws is mainly used in France and Italy Zanoli (1935) described a trans articular screw which together with a plate is fixed to the femur Putti (1938) described a simple trans articular screw without a plate Delitala (1946) and Casuccio (1946) have also designed transarticular screws The latter stabilizes with two screws which are placed at an angel to each other

In their clinical series where the fixation was done by using a trans articular screw with a femoral plate Branchiforti & Lanciotti (1957) reported 4 cases of non union out of 31 Genovesi (1964) who used a trans articular screw with or without a femoral plate sometimes in combination with osteotomy reported 32 operations and a nonunion rate of 40 per cent Cozzolino (1960) described 35 cases stabilized according to Delitala and obtained union in 94 per cent The patients were immobilized for five months Ciuccarelli & Marchi (1962) used two screws for fixation In a series of 79 cases the union amounted to 71 per cent in addition 21 per cent were relieved of pain Teinturier (1966) used 3 or 4 screws *one of* which is placed in an ischio femoral position

Schumpelik (1955) found mechanical deficiencies when stabilizing a fractured collum with a three flanged nail The nail only gave *support* at one fixed point which is the lateral layer of the cortex The author in his opinion had a superior technique of *osteosynthesis* He used a supporting coarse screw and a more cranially placed thinner screw connected to the former with a *metal plate* The upper screw is subjected to tensile stress and prevents the caput from slipping The described technique of osteosynthesis has been employed by Henssge (1967) for arthrodesis of the hip No spica is applied The author has refrained from publishing the clinical results To start with Merle d Aubigne (1962 1965) used a three flanged nail of the van Nes type but later changed to two screws and then again to three screws always in combination with plaster immobilization In calculating the percentage of *union* in relation to each technique of fixation he found that in a series of 195 operated cases there was fusion in 76 84 and 89 5 *per cent respectively*

Witt (1956) has invented his own type of double nail. A three flanged nail is inserted in a *superior-posterior direction* and then a thinner nail is introduced into a hole of the coarser nail, close to its head and at a pointed angle. The thinner nail will then be hammered into the relative centre of the acetabulum. The author believed that by using this method he could reduce the time of immobilization from between 16 and 20 weeks to between 6 *and 8 weeks. He mentioned however, that it* must not be expected that even this technique will ensure an absolute primary stabilization, due to the thin, often sclerotic, iliac bone.

Piatkowski (1959) stressed upon the unsatisfactory fixation obtained by the use of a three-flanged nail. His technique is to introduce a three-flanged *nail lengthwise into the collum* through the internal acetabular layer, and a second nail of the same type in a transversal direction. No mention is made as to the dimensions used. If nails of the conventional type are used (diameter about 13 mm) it must be difficult, sometimes impossible to fit them inside the cortex of the collum. An impairment of the bone construc*tion will result due to a large amount of the bony substance being destroyed.*

Alvik (1962) combined the three flanged nail with a plate which was formed individually at the operation and placed over the joint reaching from the anterior superior iliac spine to the ventral surface of the proximal femur. It is secured with several screws. The author kept the patient immobilized in a short hip spica *for four months,* but permitted weight bearing already after 3—4 days. In 45 cases there was no pseudarthrosis.

At osteosynthesis of a fractured femoral neck, several authors contemplated using a few thin nails for stabilization. This would mean a reduced risk of unsatisfactory nutrition and a better fixation. Nystrom (1944) thus prefers osteosynthesis with three thin *nails.* Compere & Lee *(1942)* showed by their experiments that several threaded stainless steel wires gave a very good fixation in the collum fractures. Similar experiments were also carried out by Harmon and coworkers (1948) and by Deyerle (1965). *This technique has not been used in arthrodesis to the same extent.* Blount *(1956) described the so called pin and dowel* arthrodesis. Several — four or five — pins are hammered into the greater trochanter and spread inside the ilium. Blount approved of this technique if prior to the operation, the mobility of the hip was limited. Smith and coworkers (1949) used three nails. The technique was varied inasmuch as the nails were hammered from the inside of the ilium out into the caput. The reason of this has not been expressed. Of 14 patients who were operated upon 12 united. In one patient the nail slipped into the pelvis. A number of drilled bores in the caput and the acetabulum would improve the union according to the author. In the described method the bone material is

not fully utilized to secure the nails and the resistance of the bone will become further impaired by the trauma caused by the drilling

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Schumpelik (1955) found mechanical deficiencies when stabilizing a fractured collum with a three flanged *nail* The nail only gave support at one fixed point which is the lateral layer of the cortex The author in his opinion had a superior technique of osteosynthesis He used a supporting coarse screw and a more cranially placed thinner screw connected to the former with a *metal plate* The upper screw is subjected to tensile stress and prevents the caput from slipping The described technique of osteosynthesis has been employed by Henssge (1967) for arthrodesis of the hip No spica is applied The author has *refrained* from publishing the clinical results To start with Merle d Aubigne (1962 1965) used a three flanged nail of the van Nes *type* but later changed to two screws and then again to three screws always in combination with plaster immobilization In calculating the percentage of union in relation to each technique of fixation he found that in a *series of 195* operated cases there was fusion in 76 84 and 89 5 per cent respectively

Particularly in osteosynthesis with screws it would seem necessary to utilize the multi point fixation The reason being that the circular cross section of the screw will not prevent rotation around its longitudinal axis Furthermore, the moment of inertia for a screw is less than that for a three flanged or a four-flanged nail of the same dimension Consequently, it will have a smaller resistance to bending stress The screw is superior to the nail due to its greater ability to resist tensile stress in its longitudinal axis In arthrodesis of the hip there is no stress of this type but instead the body weight and muscular force have a compressing effect The motives assigned to preferring screw reinforcement thus seem diffuse

4 Intra-Medullary Nails

Several authors have tried to perform arthrodesis with one nail into the medullary cavity of the femur According to Schneider, a long broad nail is driven in from the crest of the ilium and through this down into the femoral shaft May & Mauck (1962) using that technique had four satisfactory fusions out of six operated cases Mobilization with weight bearing began two weeks after the operation

A notable difficulty with the intra medullary methods is that the elongation of the femoral diaphysis will be lateral to the ilium Kuntscher (1957) suggested transversal osteotomy through the collum/caput and the acetabulum to obtain a better position The lower part of the pelvis and the femur will then be medially displaced and an intra medullary nail can be driven through the ilium into the femoral shaft

Dwyer (1964) also used a Kuntscher nail from the crest of the ilium into the femoral shaft He obtained medial displacement by fracturing the acetabulum and sliding in the caput In 9 cases out of 10 there was fusion One of the disadvantages of stabilization with an intra medullary nail is the difficulty of getting the nail into position Thus in three of these cases an unsatisfactory position of the hip resulted as the abduction and outward rotation was too great The author pointed out that the Kuntscher nail does not prevent movements around its longitudinal axis

Onji et al (1965) also used a straight nail which is driven in from the iliac crest into the femur Of 18 cases 16 united The authors pointed out the difficulty of getting the correct position in the arthrodesis Rutt (1958) was sceptic against the intra medullary nail and thought that it was used too often and freely His experience had been bad due to complicating *infections*

De Palma and coworkers (1962) considered the hip in its normal anatomical position as the most suitable for arthrodesis Thus they did not resect the caput nor did they perform osteotomy of the pelvis or similar

procedures The authors stabilized with a nail plate which was hammered into the femoral shaft and attached to the ala ilii with through bolts Earlier screws were used for the fixation but after a short period they detached from the ilium Of 15 cases two of which had been re-operated after an unsuccessful Schneider arthrodesis one did not unite De Palma declared that there will be compression in the arthrodesis caused by the body weight and the muscular force

5 Osteosynthesis with Compression

Several authors have insisted that union will be more rapid and secure if the osseous surfaces are subjected to compression Others inter alia, Andersson (1965) are not of the opinion that the osteogenesis would improve by compression

Compression may also contribute to better stability The osteosynthetic material has consisted of nails screws and plates

Axer (1961) and Fox (n d) have independently designed a compression nail following the same principle The nail is driven in from the greater trochanter up through the collum caput penetrating the internal cortex of the acetabulum where it is locked with a stop plate On the trochanter side the end of the nail is threaded and a plate is slipped over which rests against the cortex of the femur Then a coil spring is passed over the nail end and finally a nut is threaded on In this way there will be a continuous compression in the arthrodesis

Axer (1961) reported 19 cases Out of these 7 were further stabilized with a hip spica for two to four months According to the author immobilization in plaster is not always necessary 6 cases were re-operated In 5 cases (26 per cent) there was no fusion Fox has not published any clinical results

Langenskiold & Laurent (1967) reported a series of 13 cases operated with Axers method In 10 of these the follow up was long enough to allow assessment All of these were fused Plaster was not used and mobilization began the day after the operation Already in 1945 Niebauer designed a compression device according to the above principle (personal communication 1967)

Ostapczuk (1964) described a nail which is driven into the ilium through the acetabular roof There is a hole in the tip of the nail A pin is threaded from the outside of the ilium into the hole of the nail thus locking it A nut is used to bring about compression Five cases were operated without complications No mention is made of the rate of fusion

Mac Kee (1957) utilized a coarse screw for the osteosynthesis It is screwed into the acetabular roof The part of the screw on the femoral

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side of the joint is smooth so that it will easily slide into the bone tunnel drilled in the collum/caput By means of a plate and a nut compression is caused In view of the fact that the screw, running through the collum/caput is smooth with a circular cross section, it is unable to resist torque The clinical report is favourable, however Out of 50 operated cases 94 per cent united

Charnley (1953) also used a compression screw He tried to maintain the compression with a coil spring In his first series 13 out of 15 cases united The healing is not verified by X-ray and probably also includes what *the author calls fibrous union Morris (1962) using Charnley s* method distinguished between clinical and radiographically verified hea ling In a follow-up series of 55 cases he found union on the radiographs in 80 per cent when a plaster hip spica had been applied, and in 60 per cent when no plaster was used The clinical healing, i e abolishment of pain on the other hand, was 86 and 90 per cent, respectively Mortens & Jensen (1960) had improved patients in 33 out of 39 Only 17 of these 33 revealed fusion Charnley (1955) reported fusion in 50 per cent Debeyre (1958) stated 42 per cent and Piggot (1960) in 71 per cent

Thompson (1963) did not approve of Charnley s technique and received the statement with scepticism that the so called fibrous healing afforded as good a result as the radiographically verified fusion

A complication, following the operation according to Charnley s tech *nique is fracture of the femoral neck which by Morris (1966) was stated* to occur in 9 per cent in a series of 55 Herbert (1960) made a theoretical analysis of the forces in a normal hip and a fused hip He found that in a fused hip, the femoral neck was influenced by great forces He calcula ted the compression and tensile stress at about 250 kp/cm² when the patient stands on one leg without a nail This stress is reduced with 20 per cent using a three-flanged nail, and with 10 per cent when the nail has a circular cross section

The compression lessens and quickly disappears after the operation Charnley found that without spring loading the compression had dis appeared already during the first post operative days Morris stated that also the spring loaded compression screw lost its effect during the first post-operative weeks Rydell s investigation (1965) revealed that the caput is subject to considerable stress even when the patient lies in bed because of the muscular activity required to *lift the healthy leg for instance Thus* compression develops in the joint without any special device Pelvic osteotomy and compression belong to the method elaborated in Switzer land and designated the AO technique (Muller 1953 1967 Gertsch 1966) After performing osteotomy in the upper edge of the acetabulum

a plate is screwed to the outside of the ilium The plate contacts the lateral side of the chiselled greater trochanter and the proximal femoral shaft The plate is shaped individually at the operation if necessary No plaster immobilization is used and after three weeks mobilization begins The clinical results have not yet been published The great problem here as in the earlier mentioned intra medullary methods is to obtain the desired position of the arhtrodesis No mention is made of the difficulty in achieving a satisfactory attachment of the screws in this weak part of the ilium with its thin cortical layers This also applies to other methods where plates are used for stabilization

Stone (1956) applied a simple plate across the cranial part of the joint down to the greater trochanter The plate is supposed to give compression He immobilized for four months in plaster The author reported good clinical results with a union rate of 95 per cent in an operation series of 41 cases Daubenspeck (1966) screwed two plates to the upper part of the joint and used immobilization for six weeks He believed that compression in the joint occurred by the spring load of the plates

6 Other Methods

A method which completely differs from those earlier mentioned has been elaborated by Kirkaldi Willis and coworkers (1958) The caput is fixed to the pelvis with a staple over the joint A singular staple is from the mechanical points of view an unsatisfactory solution to the problem of stabilization The forces arising will be transferred to a very small part of the bone with too great a stress in the bone as a result The clinical results stated at a fusion rate of 54 per cent in a series of 37 cases also suggest unsatisfactory stability

[illegible]

... Charnley ... [illegible] ...

[illegible] ... Harr... ([illegible]) ... normal hip and ... [illegible] ... was inflamed ... [illegible] ... compression and tensile stress ... [illegible] ... stands on one leg without a nail. This stress is reduced ... using a three-flanged nail and with 10 per cent when ... area of cross section.

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IV Subtrochanteric Osteotomy in Arthrodesis

The osteosynthesis in arthrodesis of the hip will be subject to great stress because of the long lever formed by the femur One way of increasing the relative stability of the osteosynthesis would thus be to eliminate the lever This idea has caused several authors to suggest shortening of the lever by subtrochanteric osteotomy

F R *Thompson (1956, 1961) is spokesman for this He claims that* following arthrodesis of the hip the femur with the caput acting as a fulcrum has a lever effect of 23 1 The shaft is approximately 35 cm and the radius of the caput approximately 1 5 cm (cf Figure 1 a) By merely stating these figures a correct assessment of the problem cannot be made This relation 23 1, is furthermore incorrect The centre of the caput does not act as a fulcrum but instead the mechanical model beam with built in end is applicable Loading of the femur will cause both bending moment and torque of the nail Provided that the collum/caput is fixed with a nail in the longitudinal direction of the collum, Fig 1 b illustrates that in subtrochanteric osteotomy, the eliminated lever will be shorter than the 35 cm calculated by Thompson However the full effect of the muscular force has been neglected here In subtrochanteric osteotomy the adductors and the dorsal flexors as well as the rectus femoris muscle and the major gluteal muscle are eliminated but the medium and minor gluteal muscles the short rotators and also the iliopsoas muscle still act (cf Fig 2)

Originally, osteotomy was suggested in cases of tuberculosis Abbott (1931) described a technique where the hip was widely abducted to make the adductor muscles cause compression Correcting osteotomy was performed at a second operation and the position was gradually adjusted This technique was especially adopted for children with tuberculosis Farkas (1939) used osteotomy in cases of tuberculosis in the hip to achieve a more rapid healing

Blauth & Mau (1960) reported in a series of 21 cases 9 cases of non *union 4 of which in the hip 2* in the osteotomy and 3 both in the hip and the osteotomy They considered it disadvantageous that two operations must be performed and that the time of immobilization is long (4 months) and the shortening of the *leg pronounced (3 7 cm on an average)*

King (1952) performed osteotomy to correct the position He used a plate for internal fixation to avoid a hip spica Lange (1958) also regarded

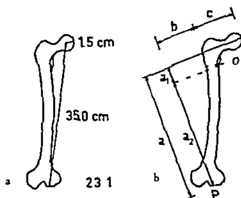


Fig 1 a The leverage 23 1 is supposed to be eliminated at subtrochanteric osteotomy (According to F R Thompson)
Fig 1 b a = leverage for torsion around nail reduced by a at subtrochanteric osteotomy
b = eliminated part of leverage for bending moment in subtrochanteric osteotomy
P = the assumed point of action of force O = place of osteotomy
N B Only the leverages in the frontal plane are calculated

the osteotomy as important to correct the position and to reduce the risk of adduction appearing in the arthrodesis

The main indication for osteotomy is to reduce the mechanical stress Wilkinson (1946) Cholmeley (1956) and Thompson (1956) suggested this as a routine procedure in arthrodesis of the hip The latter reported a series of 34 cases on which osteotomy was carried out at a rate of non union amounting to 12 per cent 3 in the arthrodesis 1 in the osteotomy In a comparative series of 20 cases without osteotomy the rate of non union was 70 per cent! Internal fixation was not used The author mentioned that non union in the osteotomy is difficult to treat but that it is a rare complication When the paper was read it was criticized by Smith who pointed out that osteotomy possibly eliminated the stress in the arthrodesis for some time The reduced stress may disappear early if the osteotomy heals He stated that in his own series he obtained union in 87 per cent without osteotomy In a series of 103 patients who were arthrodesed according to different methods Williams (1962) reported unsuccessful results in 60 per cent using ileo femoral grafting Osteotomy reduced this figure to 23 per cent

Lipscomb & Mc Caslin (1961) published the series from the Mayo Clinic They recommended Thompson s technique and a full length hip spica for four months Then mobilization with a short spica for two more months Of the patients treated according to this schedule the majority did not regain more than 70 degrees of flexion in their knee The average

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according to the above technique one did not unite while in a series of 33 cases without osteotomy fusion did not occur in 20 cases Guilleminet and coworkers (1965) performed arthrodesis according to Davis method with a pedicle crista graft The authors stated that it is not necessary to perform osteotomy as a routine

Morris (1962) published a series operated upon according to Charnley s technique He believed that osteotomy may reduce stress in the arthrodesis and thus increase the rate of fusion but that it may not reduce the time required for immobilization in plaster and for the union Hobler (1964) also was of the opinion that osteotomy will not guarantee a shorter healing period or union at a higher rate There is a great risk that non union will occur in the osteotomy if the arthrodesis fuses Jones & coworkers (1956) advocate that osteotomy causes further problems and doubted whether the osteotomy by eliminating mobility and stress in the hip can accelerate fusion of the joint In these authors view the osteotomy heals prior to the arthrodesis

Nixon and coworkers (1962) reported 13 cases operated according to Davis technique In 2 cases the arthrodesis did not unite and in 1 case the osteotomy Stabilization was carried out with plaster for about 15 weeks but without nailing 6 of the patient could flex their knee at a maximum of 90 degrees Decoulx (1965) modified Davis technique and had 2 cases of non union out of his 10 patients operated upon

Genovesi (1964) followed up 32 cases of arthrodesed hip where stabilization was done by means of one or two trans articular screws In 29 cases osteotomy was performed and 11 cases of non union resulted (38 per cent) Cauchoix (1965) published a series of 95 cases in 22 of which osteotomy was performed In the entire series there were 15 cases of non union one of which in the osteotomy Out of the 14 non united 4 belonged to the group subjected to osteotomy The rate of non union in the group of osteotomy will thus be 22 7 per cent In the group where no osteotomy was performed the percentage was 13 6

Summing up the opinions are extremely controversial with regard to the results and the advantage of osteotomy When intertrochanteric osteotomy has been performed as the only procedure in osteo arthritis of the hip a rate of non union amounting to between 12 and 13 per cent is reported despite internal fixation (Crellin & Simurda 1965 Rousborough & Stiles 1967 Scott 1967 Hirsch & Goldie 1967) The risk of non union ought to be greater in subtrochanteric osteotomy which is performed as a supplement in arthrodesis of the hip where merely a hip spica is used for the stabilization By introducing osteotomy in arthrodesis of the hip attempts have been made to solve one problem — by creating another

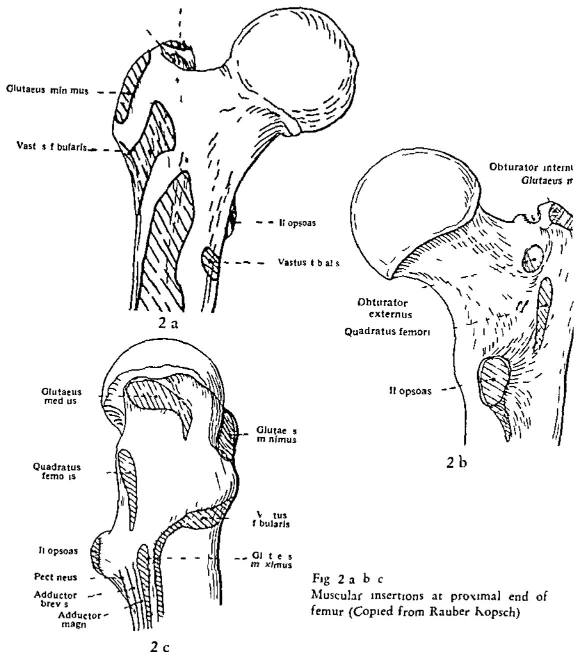


Fig 2 a b c
Muscular insertions at proximal end of femur (Copied from Rauber Kopsch)

rate of fusion was 81 per cent without osteotomy and 88 per cent with osteotomy

Apley & Denham (1955) stabilized with a three flanged nail and performed subtrochanteric osteotomy with traction treatment for six weeks Then the patient was allowed to move about with a short hip spica for another six weeks The advantage of osteotomy was expressed as follows

Movement is thus transferred from a site where bone union is difficult and doubtful to one where it is easy and probable Out of 23 cases treated

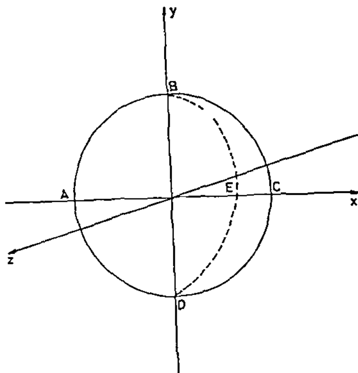


Fig 3 Three axes coordination system with measuring points A B C and points D and E for which values are calculated

superior iliac spine through the centre of the caput positive values are calculated superiorly The origin of the coordinates is assumed to lie in the centre of the caput x values are calculated as positive in an anterio medial direction A z axis is imagined from the origin towards the acetabular centre and is thus assumed to lie at an angle of 90 degrees against the other axes Its values are calculated as positive from the orgin in a lateral direction Right sided specimens were used

In the xy plane three fixed measuring points are placed at the acetabular edge as follows

A) (—R O O)
B) (O R O)
C) (R O O)

In addition two points are defined

D) (O —R O)
E) (O O —R)

The latter values are calculated on those measured in A B and C

Part II

OWN INVESTIGATIONS

General Aspects

The shape and physical properties of the reinforcement and of the object which is to be fixed, are decisive for the stability In arthrodesis of the hip it is thus the anatomical structure and the physical properties of the bone as well as the technical data of the osteosynthetic appliance which determine the efficiency of the osteosynthesis

The conditions afforded by the bone are set The appliance can be adapted to suit different demands Without doubt it is possible to achieve resistance of the appliance which would be superior to that of the bone The weakness in the construction will thus be the bone Consequently, the appliance must be designed so that the bone can carry a maximum of the transferred forces This is done by avoiding stress concentration and distributing it in as large an area as possible

The bone is a visco elastic material The deformation depends on the magnitude, speed and duration of the load (Sedlin 1965 Sedlin & Hirsch, 1965) If a certain load is exceeded, a longstanding deformation may occur and with even heavier loads fractures may result The prospects of a stable osteosynthesis will then be considerably impaired This means that there will be greater movement between the bone surfaces which are to be fused The effect of the osteosynthesis is no longer the desired

The extent of mobility between the articular surfaces in the arthrodesed hip when loading the femoral diaphysis has in thi investigation been used to determine the degree of stability On this basis an experimental technique has been elaborated

Theoretical Basis of Measuring Technique

When elaborating the measuring technique the acetabulum has been regarded as the inside of a hemisphere in which the caput articulates The caput is regarded as a sphere its radius is assumed to be R (Fig 3)

A perpendicular coordination system is placed so that the xy plane will cover the edge of the acetabulum with the y axis passing from the anterior

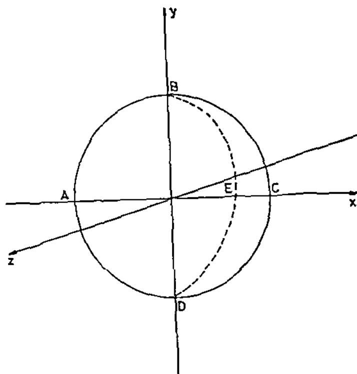


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The rotation of the caput is determined also in components around the respective axes

$\widehat{Z}$ $$p = \frac{c_1 - a_1}{2}$$

$\widehat{X}$ $$q = b - \frac{a + c}{2}$$

$\widehat{Y}$ $$r = a - \frac{a + c}{2}$$

p q and r are defined as a rotation movement around each axis at the distance R from the centre They are calculated as distances and bound to the xy yz and xz plane through the centre

For point D the translation along the x and z axes will be

$$d_1 = b_1 + c_1 - a_1$$
$$d = a + c - b$$

Point E is calculated in the respective directions of the axes

$$x = x_0 - r \quad y = y_0 + q \quad z = z_0$$

$$x_E = b_1 + \frac{c_1 - a_1}{2} - a + \frac{a + c}{2}$$

$$y_E = \frac{a_1 + c_1}{2} + b - \frac{a + c}{2}$$

$$z_E = \frac{a + c}{2}$$

The relative movement between the caput and the acetabulum in the given points is obtained by compiling the measured and the calculated co ordinates In points A B C and D the movement is calculated in the plane to which the two coordinates belong

$$S = \sqrt{s_1 + s}$$

In point E the translation will consist of movements in all the co ordinate directions

$$S = \sqrt{x + y + z}$$

The movement in each point is obtained as follows

$$S_A = \sqrt{a_1 + a}$$
$$S_B = \sqrt{b_1 + b}$$
$$S_C = \sqrt{c_1 + c}$$
$$S_D = \sqrt{d_1 + d}$$
$$S_E = \sqrt{x_E + y_E^2 + z_E}$$

Thus comparative figures have been obtained for the movement be

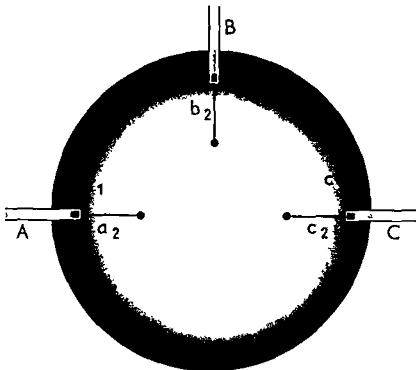


Fig 4 Direction of measurements for each gauge a_1 a b_1 b c_1 c Measuring point B placed at the acetabular edge below the anterior iliac spine

Calculations

A body of the assumed shape and with the described initial position can be subjected to rotation and translation This means that the caput can turn in or slip out from the acetabulum

The changed positions between the caput and the acetabulum due to load, are measured in the points A B and C In each point the movement is recorded in two planes Point A xy xz point B xy yz point C xy, xz The measured magnitudes are designated a_1 a b_1 b c_1 c_2 (Fig 4)

The centre of the caput is designated T (x_0 y_0 z_0) Thus the initial position coincides with the origin The translation along the respective axes is calculated accordingly

$$z_0 = \frac{a + c}{2}$$

$$x_0 = b_1 + \frac{c_1 - a_1}{2}$$

$$y_0 = \frac{a_1 + c_1}{2}$$

Experimental Device

The described calculation method is based upon certain measured data These have been obtained by the use of a specially designed experimental device It consists of a stand on which the specimen is mounted in the desired position The arthrodesis can be done using the osteosynthetic technique to be tested The device also has measuring and recording equipment The measuring component shows the distance deviation between one point on the acetabular edge and the corresponding points on the femoral head The measuring is done in the earlier defined points A B and C and in each of these performed in two planes One is a joint plane for the three points and consists of the earlier defined xy plane The measuring is thus performed along the acetabular edge and in perpendicular planes to this measuring direction i e in points A and C in the xz plane and in point B in the yz plane

Mounting the Specimen

The stand consists of four iron corner columns which are mounted in a cement foundation and at the top joined by a sturdy metal plate (Hirsch 1951) Between the columns displaceable beams are placed in the vertical plane On these beams a thick wooden board is fitted with sturdy screw joints The board is adjustable The pelvic specimen is fixed to the board with three sturdy through bolts (Figs 5 and 6)

A swivel arm is fitted at right angles to each column of the stand Between these arms there is a cross beam with a pulley in which the load wire runs The load can be applied to affect the desired directions flexion abduction extension and adduction On the swivel arms fitted to the columns there is a supporting arm system which carries the mechanical unit and the extensometers This system is designed to allow adjustment of the extensometers

Application of the Load

The load is applied to the femur in the horizontal plane (Fig 7) The point of application is set at a *fixed distance* from the upper edge of the caput to a point on the femur The distance is measured by means of a

tween the caput and the acetabular surfaces in each measured point The essential for the futher study is the maximum movement, measured to be $S_{(A-F)\ max}$ This value is selected and used with the designation S_{max} in the movement loading diagrams The diagram is obtained by plotting the S_{max} as a function of the load

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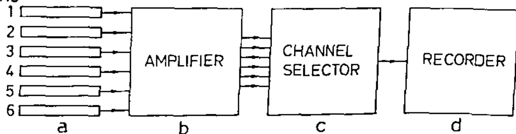
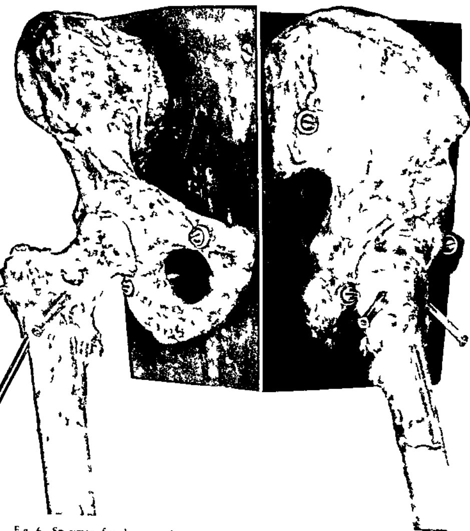


Fig 5 Photo and diagram showing experimental device Letters on diagram correspond to letters on photo



F g 6 Sp cimen f tted to wooden board F xation of h p w th th ee [illegible] Nyst om nail Frontal and la eral ews.

specially designed measuring plate of transparent plastic In the [illegible] of the plate there is a hole through which a pin slides perpen[illegible] the plate The plate is held in a vertical position The pin [illegible] directed towards the upper ed[illegible] of the caput The lower [illegible] plate will then indicat the poin at which the load[illegible] applied The leverage has t us been kept constant

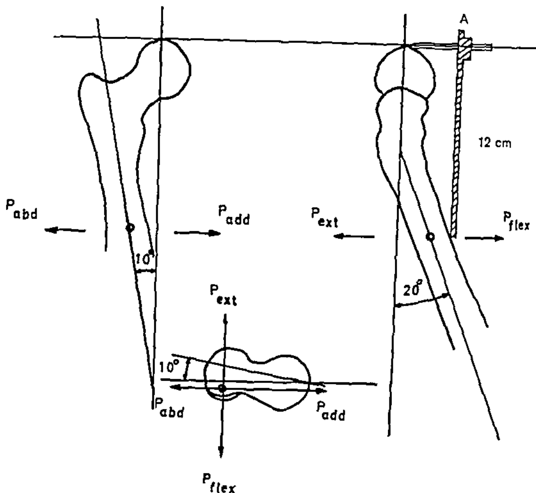


Fig 7 *Position of femur and application of load*
A indicates device for determining point for application of load

Position of Specimen

The specimen was adjusted to correspond to the pelvis of an individual in a standing position As it was impossible to obtain specimens consisting of the entire pelvis and both femurs, the individual variations could not be considered Instead certain fixed angles and distances were decisive for the adjustment of the pelvic specimen as well as the joint

the angle between the horizontal plane and a line from the promontorium through the upper end of the symphysis — 60 degrees

the angle between the sagittal plane through the symphysis and a sight line between the upper end of the symphysis and the anterior part of the sacro iliac joint — 30 degrees

the angle between the horizontal plane and a sight line in the frontal plane from the upper end of the sym physis to the anterior superior iliac spine	35 degrees
the acetabular angle according to Sharp (1961)	32—38 degrees
the transverse diameter 13 5 cm	
the angle between the longitudinal axis of the femur and	
the sagittal plane	10 degrees
the frontal plane	20 degrees
anteversion of the collum	12 degrees

(Data from Rauber Kopsch 1952 Weinreich 1959 Her bert 1960 Backman 1957 S t Claire Strange 1965)

The frontal plane of the specimen has been adjusted parallel to one of the sides of the stand

Measuring and Recording Equipment

Calipers

To measure the movement between the acetabulum and the femoral head, six calipers have been used (Fig 8) The ratio of these is 1 1 and thus the movement between the measuring tips corresponds to the movement occurring in the gauge which is placed between the opposite ends of the caliper All the joints of the measuring devices are fitted with ball bearings The calipers are assembled in pairs with a slightly elastic coupling and fitted in a specially designed frame They are placed at right angles to each other The leg of one of the calipers is soldered to the leg of the other using a thin sheet of metal At the angle of this sheet of metal there is a common tip This permits slight angular motion between the calipers The free leg of the feeler gauge is cylindrical and its tip is fitted to a spring loaded piston which is movable in this cylinder This is to secure a reliable contact with the specimen (Fig 9)

The joint measuring tip makes contact with a measuring point on the acetabulum This consists of a sheet of metal, which is screwed to the pelvis and has a free end protruding from the acetabular edge The free end is bent towards the surface of the caput so that the measuring tips will lie almost in the same plane The sheet of metal is covered with a thin layer of plastic to prevent the caliper from sliding against the metal The free measuring tip is pressed against the surface of the caput

An elastic band stretched between the frame and the specimen guarantees a continuous slight pressure between the measuring tips and the base

Displacement Gauges

The transducer used is a differential transformer manufactured by Svensk Elektronikkonsult (AB Detektor) Goteborg It is identical with that described by Rolander (1966)

The transformer consists of windings on a teflon bobbin inside which there is a movable soft iron core with a brass shaft and a measuring pointer of antimagnetic stainless steel The length of the gauge is 40 mm with an external diameter of 8 mm The transducer is wound as a balanced bridge and because of the electrical design it is possible to calibrate against a constant precision resistance The linear deviation within the measuring

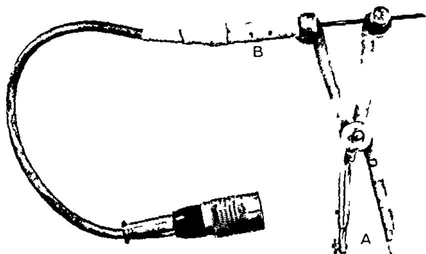


Fig 8 A Caliper B Displacement gauge

Fig 9 Detail of calipers contacting the caput and measuring points of the acetabulum

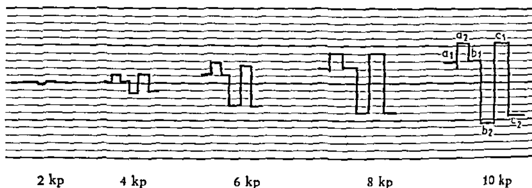


Fig 10 Original loading diagram The letters correspond to the respective gauges

range is less than 1 per cent The transducer has been regularly calibrated with a micrometer in the apparatus, designed by Rolander (1966)

Recording Device

The six transducers are connected to a specially designed switch monito (AB Svenska Philips och Svensk Elektronikkonsult, Goteborg) Each trans ducer is manually connected in turn to a carrier frequency system (Philips BF2) Each channel has its own unit for balancing and zero setting an amplifier and a calibration resistance The carrier frequency system is connected to a one-channel potentiometer recorder (*Philips PR 2210 A 21*) These devices have been described by Rolander (1966) (Fig 5)

After connecting each channel the recording paper is fed manually once a stabilized position is obtained Recording of each channel takes 2—3 seconds and for all six transducers 15 seconds Each loading and recording period thus requires 30 seconds The aim is to maintain this time constant in view of the visco elastic properties of the bone Besides the magnitude and the speed of the loading, the degree of deformation is dependent on the loading time (Sedlin 1965)

The sensitivity of the extensometer is adjusted so that a change in di stance of 1 mm between the measuring tips corresponds to 20 scale lines on the recorder The measuring error is 0 25 per cent at full scale deflec tion (full scale deflection = ±2 5 mm) The width of the recording paper is 250 mm (Fig 10)

Material

The specimens were obtained at routine autopsies at the Pathological Institute of the University Hospital and in exceptional cases at other hospitals in Goteborg They consisted of the right half of the pelvis and the

upper part of the femur including the intact hip joint and at least 15 cm of the femoral shaft Only macroscopically normal specimens were selected from cases without any general disease of the skeleton All specimens were x rayed and no abnormal signs were observed except slight osteoarthritic changes The specimens were stored at minus 30 degrees C packed in air tight plastic bags This way of storing does not affect the physical properties (Frankel 1960 Sedlin 1965 Sedlin & Hirsch 1965)

In order to assess the magnitudinal variation of the specimen certain measurements were taken Thus the maximum and minimum diameters of the collum and the diameters of the caput were noted Furthermore the body of the iliac bone was measured at its thinnest part The results are tabulated (Table III)

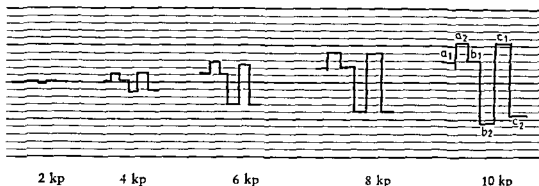


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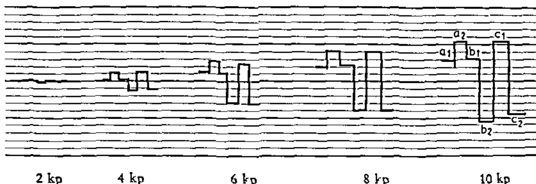


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TABLE II

The study group

Subject number	Autopsy number	Age (years)	Sex	Main cause of death
1–22	*These specimens were used for developing the methodology and for preleminary experiments*			
23	I 928	54	F	Pyelonephritis chron
24	I 980	88	F	Embolise pulm
25	I 991	45	F	Carcinoma colli uteri insuff cordis
26	I 992	49	M	Circulatory failure
27	I 898	50	M	Uremia
28	I 940	65	M	Carcinoma of the lung
29	I 919	64	F	Information missing
30	I 936	56	F	Cerebral hemorrhage
31	I 1001	66	F	Cerebral tumor
32	I 981	79	M	Bronchopneumonia
33	I 949	68	M	Cardiac failure
34	I 967	74	M	Respiratory failure
35	II 173	54	M	Bronchial carcinoma
36	I 923	64	M	Myocardial infarction
37	I 932	53	F	Uremia
38	I 736	75	F	Myocardial infarction
39	I 443	24	M	Bronchopneumonia
40	I 933	70	M	Cardiac failure
41	I 930	60	F	Cirrhosis
42	II 213	52	M	Carcinoma of the stomach
43	I 1047	59	F	Cardiac failure
44	I 1039	82	F	Cardiac failure bronchopneumonia
45	I 1032	64	F	Uremia
46	II 225	82	F	Gastrointestinal bleeding
47	I 1109	52	M	Cardiac failure
48	I 1103	59	F	Leukemia
49	I 1089	68	F	Myocardial infarction
50	I 1091	36	F	Fractur of the skull contusio cerebri
51	II 212	85	F	Pulmonary embolism
52	I 1042	71	M	Cardiac failure
53	II 201	87	M	Myocardial infarction
54	L 91	85	M	Gastrointestinal bleeding
55	I 1164	81	F	Pulmonary oedema
56	I 1158	55	F	Carcinoma colli uteri
57	II 248	69	M	Pulmonary embolism
58	I 1172	82	F	Ciculatory failure diabetes mellitus
59	I 1173	64	M	Pulmonary embolism
60	II 256	88	F	Myocardial infarction
61	L 95	75	M	Pulmonary embolism
62	I 1231	72	F	Circulatory failure
63	II 252	84	F	Circulatory failure carcinoma pancreatis
64	I 1242	79	M	Pulmonary oedema carcinoma prostatata

Subject number	Autopsy number	Age (years)	Sex	Main cause of death
65	L 97	85	F	Circulatory failure bronchopneumonia
66	II 244	69	M	Circulatory fa lure
67	I 1248	78	F	Cerebral hemorrhage circulatory failure
68	I 1246	91	F	Cerebral hemorrhage
69	II 266	56	M	Carcinoma of the stomach
70	II 245	47	F	Mal gnant lymphogranuloma
71	L 92	63	F	Circulatory fa lure bronchopneumonia
72	I 1247	8	M	Pulmonary embolism
73	I 1179	83	M	Gastrointestinal bleed ng
74	I 1302	71	M	Ci culatory failure tbc pulm
75	I 1292	62	F	Pulmonary embolism
76	II 280	50	M	Gastrointestinal bleeding pulmonary embolism
77	I 1317	53	F	Respiratory failure malignant tumor
78	L 100	62	M	*Sarcoma*
79	L 103	86	F	Circulatory failure
80	I 994	81	M	Myocardial infarction
81	L 82	59	M	Subdural bleeding
82	L 83	69	M	Circulatory f lure bronchopneumonia
83	L 83	69	M	Ci cul tory failure bronchopneumonia
84	L 77	87	M	Bronchopneumon a
85	L 77	87	M	Bronchopneumonia
86	I 1181	63	M	Myocardial infarct on
87	I 1188	55	M	Ca cinoma of the hepar
88	L 102	88	F	Bronchopneumonia
89	I 1292	73	F	Ce ebral hemorrhag
90	I 1296	55	F	Urem ia pneumonia
91	I 1335	72	M	Mal gnant tumo
92	I 1332	71	M	Cer bral m la ia
93	I 1326	51	F	Cer br l hem r hage
94	II 307	83	F	Circul tory failu e
95	I 937	62	F	Myocard l infa ct on
96	I 1334	73	M	Myocardial infarct on
97	L 103	78	F	Pulmonary embol sm
98	I 1346	89	F	Circul ory fa lure
99	I 1433	77	M	B onchopneumonia
100	I 1335	87	F	U mia ereb l oedema
101	I 1337	6	F	Carc noma of the ut rus
102	L 107	64	M	Circul tory f lu e
103	I 1336	53	F	U emia
104	I 1425	80	F	P lmonary embol sm
105	II 333	58	F	Card ac f lure
106	I 1450	(	M	Ca d c f lure
107	I 143	76	M	Pneumonia ca cinom of the stomach
108	II 11	62	M	Malignant melanoma
109	I 1442	81	F	Pericard tis
110	I 938	63	M	Mal gnant tumor
111	I 11	2	F	Ciculatory f lu e intestinal gangrene
112	I 213	67	M	Cardiac fa lure

Statistical Analysis

The statistical analysis is an assessment of the tested osteosynthetic methods with regard to the measured value S_{max}. This value has been measured under four types of loading, flexion, abduction, extension and adduction. The study was performed on a number of specimens designated No 23—112 (Table III). No values were however, obtained for specimens No 43 and No 46, because of damaged specimens.

The magnitude of the load varied between 2 and 20 kp. It was not constant for all specimens, but depended on the magnitude of the measured displacement.

In 11 cases more than one loading series was carried out with the same osteosynthetic method. On statistical analysis of these cases the values from the original experiment were used.

The following conditions complicate a statistical analysis of the present material where the intention is to elucidate the differences in the efficiency of the methods.

1. There are great variations in the physical properties of the individual specimens.

2. A non measurable weakening may occur in the specimen after testing one method of osteosynthesis. This has an impairing effect on the conditions obtained during investigation of a subsequent method.

3. Certain experiments have been performed with different load intervals and also with different maximum loads. It is impossible to concentrate the measured value obtained for the different loading directions into one adequate expression.

An attempt has been made to overcome these difficulties by statistically analysing the material in two different ways with subsequent comparison of the results.

Sign Test

The series of experiments in which two or more methods were tested on the same specimen was studied using the so called sign test.

The measured values for the respective loading directions found at the same load for two different methods on the same specimen were recorded. One of the methods was used as a reference and the sign of the difference

TABLE III

Experiments

Number of specimen	Method	Diameter of the acetabulum mm	Width of the femoral neck min. mm	Width of the femoral neck max. mm	Min. width of the body of nail mm	Angle between nail and femoral shaft degrees	Nailing depth mm
23	Sv J	45	26	32		145	24
24	Sv J	40	22	30		145	36
25	Sv J	45	27	39	22	145	20
26	Sv J	50	28	40	30	145	18
27	Sv J	51	31	40	30	145	21
28	Sv J	52	31	39	32	140	34
29	Sv J	50	30	40	30	150	32
30	Axer	55	30	40	28	130	25
31	Axer	46	25	33	24	135	14
32	Axer	54	30	38	25	130	14
33	3pfix N	47	23	30	24		
34	3pfix N	50	25	32			
35	3pfix N	50	27	37	24		
36	Axer	50	30	38		130	17
37	Axer	50	25	36		130	11
38	Axer	53	29	43		135	17
39	Sv J	44	26	32	18	150	18
40	Sv J	53	32	37		150	34
41	3pfix N	50	27	32	23	145	30
42	Sv J	50	29	43	26	145	38
43	Sv J	45	28	31		150	43
44	Sv J	48	26	32	26	145	40
45	3pfix, N	46	26	34	23		
46					26		
47	Sv J	48	30	37		145	30
48	Sv J	45	26	37		150	47
49	Sv J	44	26	31		153	45
50	Sv J	46	26	30		152	49
51	Sv J	45	26	30		152	54
52	Sv J	49	30	34		143	34
53	3pfix N Sv J	49	25	34	25	147	47
54	3pfix N	50	26	34	23		
55	3pfix N	47	26	32	22		
56	Sv J 3pfix N	45	24	32	22	150	20
57	Sv J 3pfix N	54	30	38	28	150	33
58	3pfix, N	43	23	31	25	150	31
58	3pfix, N Sv J	43	23	31	25	150	31
59	3pfix N Sv J	52	28	36	25	145	40
60	3pfix, N S J Sv J + plate	51	29	35	31	140	53

Sv J = Sven Johanson three flanged nail
N = Nystrom nail
E = Experimental nail

N mber of pe m	M thod	D m t of the a eta b lum mm	k th f femo al m mm	k m mm	M w d h of th body of l m mm	Ang! be t een l d f mor l haft d gree	N d p h mm
61	3pfix N	49	29	34	28	135	6/
	Sv J						
	Sv J + N						
	Sv J + Plate						
62	3pfix N	45	25	30		140	29
	Sv J						
	Sv J + N						
	Sv J + Plate						
63	3pfix N	44	24	33	26	150	60
	Sv J						
	So J + N pos III						
	Sv J + N pos II						
	Sv J + Plate						
64	3pfix N	50	26	36	25	140	(6
	Sv J						
	Sv J + N pos II						
	Sv J + N pos III						
	Sv J + Plate						
65	Fox	48	28	37	24	140	19
	3pfix N						
66	3pfix N	47	25	33	25	135	11
	Fox						
67	3pfix N	44	25	32	23	14ɔ	49
	Sv J						
	Sv J + N						
	Sv J + Plate						
68	3pfix N	43	24	30	23	130	14
	Fox						
69	3pfix N	55	32	36	27	140	4(
	Sv J						
	Sv J + N pos II						
	Sv J + N pos III						
	Sv J + Plate						
70	3pfix N	43	27	33	22		
71	3pfix N	46	25	31	23	130	1(
	Fox						
72	3pfix N	53	29	40	_5	148	4(
	Sv J						
	Sv J + N pos II						
	Sv J + N pos III						
	Sv J + Plate						
	Fox					135	11
73	3pfix screws	60	33	42	30	140	32
	3pfix Sv J mod						
74	3 pfix screws	52	34	39	_4	13	23
	3pfix N						
	3P Sv J mod						
	Sv J + N						

N mbe f specimens	Method	Di met of he et bal m mm	W d h of femoral ne k m n. mm	W d h of femoral ne k max. mm	M n. wid h f th bod f ali m mm	A gl be tw en nd nd f moral h. f degrees	N ling dep h mm
75	3pfix scr ws	44	2(	30	22	140	17
	3pfix N						
	3pfix Sv J mod						
	Sv J + N						
	Sv J						
(	Fox	49	30	35	26	135	20
	3pfi Sv J mod					135	32
77	3pfix sc ews	50	29	33	24	140	27
	3pfix N						
	3pfix Sv J mod						
78	3pfix screws	4	27	32	24	145	57
	3pfi (rep)						
	3pfi Sv J mod						
9	Mc L	53	30	37	31	150	52
	Mc L						
	Mc L osteotomy						
	Mc L + N						
	Mc L + N						
80	Axer	50	29	35	21	145	50
	S J						
	Sv J + N						
81	Axer	49	29	37	22	135	22
	Sv J + N						
82	Sv J mod	54	35	40	19	140	40
83	Sv J	54	32	38		140	30
84	E	50	27	36		135	46
85	Sv J	49	29	34		135	45
86	3pfix N	55	32	39		145	17
	Mc Kee						
8	3pfi N	51	31	36		135	30
	M K						
88	3pfix N	42	26	32		145	26
	Mc Kee						
89	3pfi N	45	26	32		135	22
	3pfix N mod						
	Mc Kee						
90	3pfix N	42	28	32		140	41
	3pfi N mod						
	Mc Kee						
91	3pfi scr w	50	29	35			
	3pf N						
	3pf N mod						
9	3pfix screw	50	26	35			
	3pfi N						
	3pf x N mod						
93	3pfix screw	48	26	31			
	3pfix N						
	3pfix N mod						
94	3pf x sc ew	49	26	35		140	25
	3pf x N						

N mb of pe m n	M th d	D a n t of th ta b l m mm	W d h f femo l neck m n mm	m mm	M n w dth of th b dy of il m mm	A gl be twee l a d femoral h ft d g ee	N d pth mm
61	3pfix N	49	29	34	28	135	67
	Sv J						
	Sv J + N						
	Sv J + Plate						
62	3pfix N	45	25	30		140	29
	Sv J						
	Sv J + N						
	Sv J + Plate						
63	3pfix N	44	24	33	26	150	60
	Sv J						
	So J + N pos III						
	Sv J + N pos II						
	Sv J + Plate						
64	3pfix N	50	26	36	25	140	66
	Sv J						
	Sv J + N pos II						
	Sv J + N pos III						
	Sv J + Plate						
65	Fox	48	28	37	24	140	19
	3pfix N						
66	3pfix N	47	25	33	25	135	11
	Fox						
67	3pfix N	44	25	32	23	145	49
	Sv J						
	Sv J + N						
	Sv J + Plate						
68	3pfix N	43	24	30	23	130	14
	Fox						
69	3pfix N	55	32	36	27	140	46
	Sv J						
	Sv J + N pos II						
	Sv J + N pos III						
	Sv J + Plate						
70	3pfix N	43	2[illegible]	33	22		
71	3pfix N	46	25	31	23	130	1[illegible]
	Fox						
72	3pfix N	53	29	40	25	148	46
	Sv J						
	Sv J N pos II						
	Sv J + *N pos III*						
	Sv J + Plate						
	Fox					135	11
73	3pfix screws	60	33	42	30	140	32
	3pfix Sv J mod						
74	3 pfix screws	52	34	38	24	13	23
	3pfix N						
	3P Sv J mod						
	Sv J + N						

Number of sne me	M hod	Diame of the ce bal m mm	W d h of f moral ne k m n. mm	max. mm	Min. wid h f the bod of al m mm	Ar gl be w en and nd femoral h f degre	N ling depth mm
ɔ	3pfix screws	44	26	30	22	140	17
	3pfi. N						
	3pfix Sv J mod						
	Sv J – N						
	S J						
6	Fox	49	30	35	26	135	20
	3pfix Sv J mod					13ɔ	32
77	3pfi. screws	50	29	33	24	140	27
	3phx N						
	3pfi Sv J mod						
8	3pfix screws	47	27	3?	24	145	57
	3pfix (rep)						
	3pfix Sv J mod						
9	Mc L	53	30	3	31	150	52
	Mc L						
	Mc L. osteotomy						
	Mc L + N						
	Mc L + N						
80	Axer	50	29	3ɔ	21	145	50
	Sv J						
	Sv J + N						
81	A r	49	29	37	22	13ɔ	22
	Sv J + N						
8?	Sv J mod	54	35	40	19	140	40
83	Sv J	54	3?	38		140	30
84	F	50	27	36		135	46
8ɔ	S J	49	29	34		135	45
86	3phx N	55	32	39		125	17
	Mc Ke						
87	3pfix N	51	31	36		135	30
	Mc Kee						
88	3pfix, N	4?	6	32		14ɔ	26
	Mc Kee						
89	3pfi. N	45	26	32		135	22
	3pfix N m d						
	Mc Kee						
90	3pfi N	42	28	3?		140	41
	3pfix N mod						
	Mc Ke						
91	3pfi screw	50	29	3ɔ			
	3pfi. N						
	3pfix N mod						
9?	3pfi screw	50	26	35			
	3pfi N						
	3pfix N mod						
93	3pfi screw	48	26	31			
	3pfi N						
	3pfix N m d						
94	3pfi sc ew	49	6	35		140	5
	3pfi N						

Number of persons	Method	Diameter of the head mm	Width of femoral neck min mm	Width of femoral neck max mm	Min width of the body of ilium mm	Angle between femoral neck and femoral shaft	Nailing depth mm
61	3pfix N	49	29	34	28	135	67
	Sv J						
	Sv J + N						
	Sv J + Plate						
62	3pfix N	45	25	30		140	29
	Sv J						
	Sv J + N						
	Sv J + Plate						
63	*3pfix* N	*44*	*24*	*33*	*26*	*150*	*60*
	Sv J						
	So J + N pos III						
	Sv J + N pos II						
	Sv J + Plate						
64	3pfix N	50	26	36	25	140	66
	Sv J						
	Sv J + N pos II						
	Sv J + N pos III						
	Sv J + Plate						
65	Fox	48	28	37	24	140	19
	3pfix N						
66	3pfix N	47	25	33	25	135	11
	Fox						
67	3pfix N	44	25	32	23	145	49
	Sv J						
	Sv J + N						
	Sv J + Plate						
68	3pfx N	43	24	30	23	130	14
	Fox						
69	3pfix N	55	32	36	27	140	46
	Sv J						
	Sv J + N pos II						
	Sv J + N pos III						
	Sv J + Plate						
70	3pfix N	43	27	33	22		
71	3pfix N	46	25	31	23	130	10
	Fox						
72	3pfix N	53	29	40	25	148	40
	Sv J						
	Sv J + N pos II						
	Sv J + N pos III						
	Sv J + Plat						
	Fox					135	11
73	3pfix screws	60	33	42	30	140	32
	3pfix Sv J mod						
74	3 pfix screws	52	34	38	24	135	23
	3pfix N						
	3P Sv J mod						
	Sv J + N						

Number of specimen	Method	Diameter of the acetabulum mm	Width of the femoral neck min. mm	max. mm	Width of the body of ilium mm	Angle between screw and femoral shaft degrees	Nailing depth mm
5	3pfix screws	44	26	30	22	140	17
	3pfix N						
	3pfi S J mod						
	Sv J + N						
	Sv J						
6	Fox	49	30	35	26	135	20
	3pfix Sv J mod					135	32
77	3pfix, screws	50	29	33	24	140	27
	3pfix N						
	3pfix Sv J mod						
8	3pfix screws	47	27	3[illegible]	24	145	57
	3pfix (rep)						
	3pfi Sv J mod						
9	Mc L.	53	30	37	31	150	52
	Mc L.						
	Mc L osteotomy						
	Mc L + N						
	Mc L + N						
80	Axer	50	[illegible]9	35	21	145	50
	S J						
	S J + N						
81	Axer	49	29	37	22	135	[illegible]2
	S J + N						
8	Sv J mod	54	35	40	19	140	40
83	S J	54	32	38		140	30
84	E	50	27	36		135	46
85	S J	49	29	34		135	45
86	3pfix N	55	32	39		125	17
	M Kee						
8[illegible]	3pfix N	51	31	3[illegible]		135	30
	Mc Kee						
88	3pfix N	4[illegible]	26	3[illegible]		145	26
	M Kee						
89	3pfix N	45	26	3[illegible]		135	22
	3pfix N mod						
	Mc Kee						
90	3pfi N	4[illegible]	28	3[illegible]		140	41
	3pfix N mod						
	M Kee						
91	3pfix screw	50	29	35			
	3pfix N						
	3pfi N mod						
9[illegible]	3pfix screw	50	26	35			
	3pfi N						
	3pfi N mod						
93	3pfix screw	48	[illegible]	31			
	3pfi N						
	3pfix N mod						
94	3pfi screw	49	26	35		140	25
	3pfix N						

Numbe of pecim n	M thod	Diamet r of th ac ta b lum mm	W dth of femoral n ck m n mm	max mm	Min. width of the body of d m mm	Angle be tween nail and f moral shaft degree	N l ng depth mm
94	3pfix N mod Mc Kee						
95	3pfix N 3pfix N mod E + N	45	26	32		140	29
96	3pfix screw 3pfix N 3pfix N mod Niebauer	50	26	33		130	12
97	Niebauer 3pfix N 3pfix N mod	48	28	37		130	16
98	Niebauer 3pfix N 3pfix N mod	45	26	32		125	15
99	3pfix N E + N	50	28	35		145	45
100	3pfix N E + N	43	26	31		145	46
101	3pfix N E + N	48	27	35		145	40
102	3pfix N E + N	50	27	34		145	44
103	3pfix N E + N	41	22	28		150	40
104	3pfix N E + N	47	26	32		145	36
105	3pfix N E + N	44	24	28		140	34
106	3pfix N E + N	53	29	35		140	35
107	3pfix N E + N	50	29	36		145	49
108	3pfix N E + N A O	52	30	41			38
109	3pfix N A O	46	25	32			
110 r	3pfix N E + N	48	26	32		145	45
110 l	3pfix N Sv J + N	49	28	32		140	40
111 r	3pfix N Sv J + N	44	24	32		150	40
111 l	3pfix N E + N	40	20	26		150	45
112	A O						

between the measured values for this and the other method was determined In this way a eries of + and — signs was obtained for various pairs of methods

On the assumption that the methods are equally good from the point of view of stability the number of + and — signs ought to be roughly the same If the number of the type of sign (+ or —) that occurs least falls below a certain limit the assumption is rejected and the difference is said to be significantly positive or negative depending on the distribu tion of the signs (Brownlee 1965) An analysis of this type requires com parison of at least six observations (Table IV) This is the reason why com parisons could not be made in certain experiments despite the fact that two methods were employed on the same specimen One method can have giver such poor stability that the required number of observations could not be made In spite of the fact that this first method was inferior to that with which it was compared it was not possible to ascertain this difference b the present method of analysi

Table X gives a survey of the results of the sign test It should b emphasized that this is a matter of isolated comparisons in pairs The tes was performed on a 5 per cent level The designation Sv J refers to case where the depth of the insertion of the three-flanged nail exceeded 30 mm

Descriptive Calculations

The following calculation was performed in an attempt to obtain full assessment of the series For each method the mean values of S_m , fc loads of 6 8 and 10 kp was calculated for the loading directions invest gated These mean values were ranked within each loading direction an for each load For each direction and load a rank sum was then calcu lated and finally a total rank sum for each method From this tota sum of ranks a mean rank sum was obtained by dividing by 12 (3 load 4 loading directions) (Table XII)

In the ranking procedure the method with the lowest mean value wa ranked 1 that with the next lowest mean value 2 and so on If the mea value happened to be identical they both received a ranking number equ to the mean value of those ranking numbers they would have receive had they been slightly different

The mean rank sum can be said to provide a quantitative measure fo a given fixation type with the following reservations

1 Variations in the physical properties of the specimens have been di regarded These variations could be rather large as is partly illustrate by the standard deviations calculated for the three-flanged nail an three point nail fixation (Table V) The standard deviation is in the

Number of specimen	Method	Diameter of the acetabulum mm	Width of femoral neck min mm	Width of femoral neck max mm	Min. width of the body of ilium mm	Angle between neck and femoral shaft degrees	Nailing depth mm
94	3pfix N mod Mc Kee						
95	3pfix N 3pfix N mod E + N	45	26	32		140	29
96	3pfix screw 3pfix N 3pfix N mod Niebauer	50	26	33		130	12
97	Niebauer 3pfix N 3pfix N mod	48	28	37		130	16
98	Niebauer 3pfix N 3pfix N mod	45	26	32		125	15
99	3pfix N E + N	50	28	35		145	45
100	3pfix N E + N	43	26	31		145	46
101	3pfix N E + N	48	27	35		145	40
102	3pfix N E + N	50	27	34		145	44
103	3pfix N E + N	41	22	28		150	40
104	3pfix N E + N	47	26	32		145	36
105	3pfix N E + N	44	24	28		140	34
106	3pfix N E + N	53	29	35		140	35
107	3pfix N E + N	50	29	36		145	49
108	3pfix N E + N A O	52	30	41			38
109	3pfix N A O	46	25	32			
110 r	3pfix N E + N	48	26	32		145	45
110 l	3pfix N Sv J + N	4[illegible]	28	32		140	40
111 r	3pfix N Sv J + N	44	24	32		150	40
111 l	3pfix N E + N	40	20	26		150	45
112	A O						

TABLE V

Standard deviation of S_{ma} for 3pfix N and Sv J

3pfix N					
Loading kp	6	8	10	12	14
Flexion	6,4	9,6	15,5	20,4	15,7
Abduction	5,0	7,9	13,2	18,3	28,3
Adduction	10,5	17,4	23,1	29,2	37,4
Extension	12,4	18,4	23,2	24,9	22,8
Sv J					
Loading kp	6	8	10	12	14
Flexion	23,6	17,4	13,3	18,9	24,0
Abduction	10,6	17,7	28,8	41,1	27,6
Adduction	21,2	30,4	38,2	45,1	43,7
Extension	16,1	24,9	30,3	33,4	26,4

2 The fact that different numbers of observations have been used in calculating the different mean values has been disregarded

The mean values within a certain direction of movement should of course increase with heavier loads It can be seen from the tables of the mean values for the different methods that this is not always the case however This depends on the fact that the weak specimens have been gradually excluded as the load has increased and thus not contributed to the results at higher loads (cf Table XI)

TABLE IV

Rejection limits for sign test Test level 5 per cent

N	2α = 0.05	N	2α = 0.05	N	2α = 0.05	N	2α = 0.05	N	2α = 0.05
	x_l x_r		x_l x_r		x_l x_r		x_l x_r		x_l x_r
0	—								
1	—	21	5−16	41	13−28	61	22−39	81	31−50
2	—	22	5−17	42	14−28	62	22−40	82	31−51
3	—	23	6−17	43	14−29	63	23−40	83	32−51
4	—	24	6−18	44	15−29	64	23−41	84	32−52
5	—	25	7−18	45	15−30	65	24−41	85	32−53
6	0−6	26	7−19	46	15−31	66	24−42	86	33−53
7	0−7	27	7−20	47	16−31	67	25−42	87	33−54
8	0−8	28	8−20	48	16−32	68	25−43	88	34−54
9	1−8	29	8−21	49	17−32	69	25−44	89	34−55
10	1−9	30	9−21	50	17−23	70	26−44	90	35−55
11	1−10	31	9−22	51	18−33	71	26−45	91	35−56
12	2−10	32	9−23	52	18−34	72	27−45	92	36−56
13	2−11	33	10−23	53	18−35	73	27−46	93	36−57
14	2−12	34	10−24	54	19−35	74	28−46	94	37−57
15	3−12	35	11−24	55	19−36	75	28−47	95	37−58
16	3−13	36	11−25	56	20−36	76	28−48	96	37−59
17	4−13	37	12−25	57	20−37	77	29−48	97	38−59
18	4−14	38	12−26	58	21−37	78	29−49	98	38−60
19	4−15	39	12−27	59	21−38	79	30−49	99	39−60
20	5−15	40	13−27	60	21−39	80	30−50	100	39−61

cases calculated from the expression $\sqrt{\frac{\Sigma(x-\bar{x})^2}{n}}$ where x is the deflection in the direction and load concerned $\bar{x}$ is the mean value of all x, and n the number of observations i e the number of specimens where observations were made for the different directions and loads The table reveals high standard deviations for the three flanged nail and lower ones for the three point fixation The high values probably depend on the specimen factor *) which includes in particular the variation of the physical properties of the material Also of importance are mechanical changes occurring in connection with the osteosynthesis itself The latter occur to a greater extent in osteosynthesis with the three flanged nail than with the considerably thinner N nails In addition by using three nails a smoothing effect is obtained in other words the importance of the specimen factor is greater when only one nail is used

*) Cf page 58

This creates the disadvantage of the first osteosynthetic procedure affecting the specimen in such a way that the conditions for the following ones will be impaired

To master this problem certain rules have been set The method requiring the smaller amount of bone was tried before the one engaging a greater amount i e osteosynthesis with thinner nails was performed before using the coarser ones

When it was not quite clear which method caused the least damage the succession of the methods was varied The method seeming to be the most inferior at the preliminary experiments was tried as the first method when the next series of experiments was carried out The best conditions for testing were thus given the assumed inferior method

The loading level reached at each experiment depended on the degree of deformation The intention was to evade remaining deformation The load was increased stepwise by 2 kp and normally the load was augmented to a moment of 120 kpcm before unloading The degree of remaining deformation after unloading was also recorded The loadings were always done in the same succession flexion abduction extension adduction

N B The following abbreviations will from now on be used

Three-flanged Sven Johansson nail = Sv J nail

Nystrom nail = N nail

Stabilization with Three-Flanged-Nail

Theoretical Analysis

Stabilization in arthrodesis of the hip with a three-flanged nail has perhaps been the most common method Special attention has therefore been paid to this method It is referred to in technical literature as the simple nail reinforcement and due to its simple mechanical design it can be analysed theoretically to a certain extent The purpose of this is to elucidate guiding principles for experimental application

This kind of analysis is complicated by the number of variable factors in the composition of the bone The shape of the skeleton is complicated and the bone is inhomogeneous with wide variations in the material properties These factors cannot be represented mathematically Simplifications and assumptions must be made

In the analysis a three-flanged nail of the Sv J type has been selected

Assumptions

The calculations are carried out using the mechanical model beam on elastic foundation The deflection curve of beams on spring supports can

Experimental Study

For the following osteosynthetic procedures, the previously described testing technique was employed

A Nail Reinforcements

1 Three-flanged nail according to Sven Johansson
2 *Three flanged nail* + one *Nystrom nail*
   a Nystrom nail in lateral medial direction (pos II, Fig 24)
   b Nystrom nail in an anterio-posterior direction (pos III)
3 Three Nystrom nails
   a Three of standard dimension
   b *Two of standard dimension + one coarser nail (pos I)*
4 Three-flanged nail + plate according to Alvik
5 Four flanged experimental nail + lateral medial Nystrom nail (pos II)

B Screw Reinforcement

Three trans articular *screws*

C Compression Methods

1 Compression nail according to Axer
2 Compression nail according to Fox
3 *Compression nail according to Niebauer*
4 Compression screw according to Mac Kee
5 Compression plate according to AO

Initially only one osteosynthetic method was performed on each specimen However the specimens varied considerably with respect to size and resistance (These factors have in the following been denominated the *specimen factor)* Because of this variation the experimental series would have been too extensive to ensure a statistically significant result for all the methods to be tested

By using several osteosynthetic methods on the same specimens the specimen factor can be considerably reduced Thus direct comparisons between the various osteosynthetic methods can be made

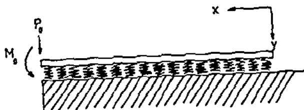


Fig 11 Model according to Case 1 (Homogeneous cortical bone)

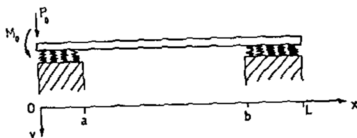


Fig 12 Model according to Case 2 (Two cortical layers with hollow intermediate space)

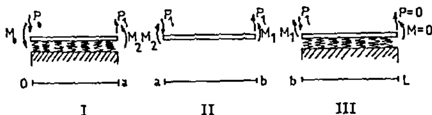


Fig 13 Case 2 divided into three parts

Calculations

Equations for each partial loading case are obtained by superposition of the elementary cases for concentrated force and moment according to Hetenyi Beams on elastic foundation By constructing boundary conditions the true deflection curve can be calculated When the form of the curve has been obtained interest is concentrated on the most critical factor for the bone material i e the point of maximum deflection

Maximum deflection is obtained in the actual loading cases at that point where the force and moment are concentrated i e at the external edge of the bone

Formulae are devised for calculation of the edge deflection as a function of the following parameters

be represented by means of a fourth degree differential equation In order to calculate the shape of the curve in a special case the existing boundary conditions are included in the general equation After solving the equation the deflection is obtained as a function of parameters, depending only on the properties of the beam — and the support The following assumptions are made

1 The bone material obeys Hook s law
2 The deflection of the material is transmitted in a finite area of the bone

The spring constant of the bone can then be calculated On the basis of these calculations, the deflection of a nail in bone material can be determined for various degrees of loading as well as the effect of the varying nail and bone properties

The nail penetrates two cortical layers which surround an area of spongy bone The material is inhomogeneous and has varying physical properties in each layer Between these layers there is no sharp boundary The elastic resistance of the spongy bone is of little importance when considering tensile and compressive stresses On the other hand the cortical bone has marked physical properties(Rauber 1876 Evans 1957 Sedlin 1965) Because of these conditions, calculations were carried out for two extreme cases, the bone material of which was assumed to be

1 Solid cortical bone (infinite homogeneous elasticity)
2 Two cortical layers with a hollow intermediate space (stepwise elasticity)

Case 1 On the basis of assumption 1 the model shown in Fig 11 is used to calculate the deflection curve In this case the deflection caused will obey the following differential equation

$$\underline{DE} \quad \frac{d^4y}{dx^4} + 4\,n^4y = 0$$

$$\text{where} \quad \frac{C}{EI} = 4\,n^4$$

C = spring constant of elastic support
EI = bending resistance of nail

Case 2 On the basis of assumption 2 above the model shown in Fig 12 is used to calculate the deflection curve

The loading case defined according to this figure with the load and moment applied to the end point is conveniently treated in parts according to Fig 13

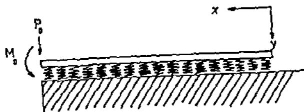


Fig 11 Model according to Case 1 (Homogeneous cortical bone)

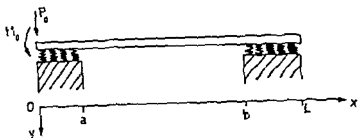


Fig 12 Model according to Case 2 (Two cortical layers with hollow intermediate space)

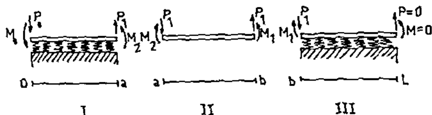


Fig 13 Case 2 divided into three parts

Calculations

Equations for each partial loading case are obtained by superposition of the elementary cases for concentrated force and moment according to Hetenyi Beams on elastic foundation By constructing boundary conditions the true deflection curve can be calculated When the form of the curve has been obtained interest is concentrated on the most critical factor for the bone material i e the point of maximum deflection

Maximum deflection is obtained in the actual loading cases at that point where the force and moment are concentrated i e at the external edge of the bone

Formulae are devised for calculation of the edge deflection as a function of the following parameters

1 Modulus of elasticity of the bone

2 Spring constant of the bone

3 Moment of inertia of the nail

4 Modulus of elasticity of the nail

1 The modulus of elasticity, E_b for cortical bone, varies within wide limits and is strongly dependent on the type of loading (Sedlin, 1965) For these approximate calculations, a mean value between the moduli of elasticity for tension and for compression has been used, viz $E_l = 1075$ kp/mm²

2 The spring constant (C) is calculated according to a special model $C = k \ E_b$ where k is a constant The value of the constant varies with certain shape factors and has been calculated to lie within the range $2\,0 > k > 1\,6$ To calculate the deflection of the edge in the acetabulum the value $k = 1\,75$ is used

3 The three-flanged nail of the Sv J-type used for calculations and experiments has a moment of inertia of 140 mm⁴

4 The nail is made of stainless steel with a modulus of elasticity $E_s = 21\,000$ kp/mm²

The Influence of Nailing Depth on Deflection of Edge

Assuming according to Case 1 (solid cortical bone) the deflection of the edge is calculated for a given force and moment as a function of the length (= L) of the part of the nail which is inserted into the material The result of these calculations shows that when a certain depth has been reached only a very slight improvement will be achieved by increasing the depth Thus, an improvement of only 5 per cent will be obtained if L is increased from 22 mm to infinite depth With decreasing nailing depth the deflection of the edge will increase rapidly (Fig 14)

Assuming, according to Case 2 (two cortical layers with a hollow intermediate space) the deflection of the edge is calculated as a function of the thickness of the cortical layers and of the distance between them

According to the principle of superposition complete calculations can be carried out for force and moment separately and the results superimposed in the final calculations

In order to obtain an unambiguously defined quantity as a result the separate deflections are related to the deflection obtained using infinite homogeneous elasticity This involves defining the quotients

for the force $R^P = \dfrac{\delta_0^P}{\delta^P_{0\,(\infty)}} = \dfrac{\delta_0^P}{\dfrac{P_0}{2n^3 \ EI}}$

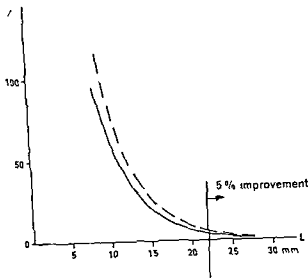


Fig 14 – – – – – – R^P ———— R^M Improvement in percentage (diminished edge deflection) with increasing nailing depth according to Case 1

for the moment $R^M = \frac{\delta_0^M}{\delta^M_{0(\infty)}} = \frac{\delta_0^M}{\frac{M_0}{2n \quad EI}}$

Calculations are performed assuming constant parameters the values of which are discussed above

E_b = 1075 kp/mm
C = 1 75 × E_b = 1880 kp/mm
n = 0 1125

The results are tabulated in Table VI The curve for a cortical layer thickness a = 2 5 mm is selected as a basis and the quotients relating the other curves to this basis curve are formed The table of force values shows that the quotients of the variables (b—a) are almost the same for each curve This implies that only the exact form of the basis curve is reported together with a comparison curve for the quotients as a function of a values (Fig 15)

The table of values of moment shows that a corresponding relation does not exist For the different a values separate curves are plotted (Fig 16) To obtain the intermediate a values interpolation has to be made

Under the assumption that the bone obeys Hooke s law the values R^P and R^M are calculated from the curves of force and moment quotients These are converted to a coefficient which constitutes the direction coef

TABLE VI

Quotients R^P and R^M at some different values for a and b−a measured in mm

$E_b = 1075$ $C = 1880$ $E_s = 21000$ $I_s = 140$

R^P

b−a	$a_1 = 0\ 8$	$a_2 = 1\ 0$	$a_3 = 1\ 5$	$a_4 = 2\ 0$	$a_5 = 2\ 5$	$\frac{R^P a_1}{K^P a_5}$	$\frac{R^P a_2}{R^P a_5}$	$\frac{R^P a}{R^P a_5}$	$\frac{R^P a}{R^P a_4}$
0									
2 5	6 937	5 802	4 161	3 292	2 743	2 55	2 12	1 52	1 0
5	6 356	5 223	3 692	2 907	2 425	2 62	2 15	1 52	1,2[illegible]
10	5 981	4 865	3 372	2 622	2 171	2 76	2 24	1 55	1 [illegible]1
20	5 778	4 667	3 187	2 452	2 016	2 87	2 32	1 58	1 2[illegible]
40	5 674	4 566	3 095	2 370	1 947	2 91	2 35	1 59	1 22
80	5 626	4 521	3 062	2 355	1 952	2 88	2 32	1 57	1 21
120	5 614	4 512	3 065	2 373	1 989	2 82	2 27	1 54	1 19
					Mean value	2 77	2 25	1 55	1 21

R^M

b−a	$a = 0\ 8$	$a_2 = 1\ 0$	$a = 1\ 5$	$a_4 = 2\ 0$	$a = 2\ 5$	$\frac{R^M a}{R^M a_5}$	$\frac{R^M a}{R^M a}$	$\frac{R^M a}{R^M a}$	$\frac{R^M a}{k^M a}$
0									
2 5	24 587	19 737	12 875	9 249	7 031	3 49	2 80	1 83	1 31
5	11 731	9 578	6 581	4 994	4 001	2 94	2 40	1 6[illegible]	1 25
10	5,545	4 538	3 181	2 494	2 082	2 66	2 18	1 53	1 20
20	2 700	2 221	1 [illegible]01	1 313	1 161	2 33	1 91	1 [illegible]8	1 13
40	1 416	1 204	0 964	0 891	0 884	1 60	1 36	1 09	1 01
80	0 902	0 847	0 856	0 946	1 064	0 85	0 79	0 80	0 89
120	0 825	0 845	0 990	1 1[illegible]3	1 386	0 60	0 61	0 71	0 85

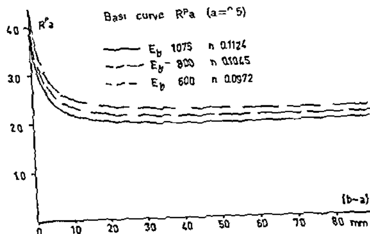
ficient in the equation which represents the deflection as a function of the force P_0

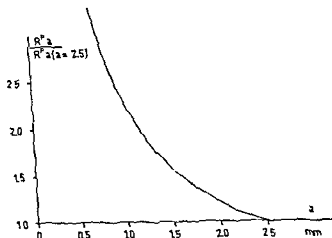
$$\delta_0 = \delta_0^{I} + \delta_0^{M}$$

$$\delta_0^{P} = \frac{R^P}{2n^3\ EI} \times P_0$$

$$\delta_0^{M} = \frac{R^M}{2n^2\ EI} \times M_0$$

M_0 is converted to $M_0 = L \times P_0$
from which is obtained $\delta_0 = (K_0^P + K_0^M) \times P_0$





F g 15 a) Basis curve for R^P and cort cal layer a = 2 5 mm
b) Cor parison cur e for the quotients as a funct on of a values

The influence on the edge deflection of a variation of the modulus of elasticity is shown in Diagrams 15 and 16 It is here seen that the values of R^P are increased by approximately 7 *per cent* when changing n from 0 1124 to 0 1045 The R^P values are increased by approximately 15 per cent when changing n from 0 1124 to 0 0972 These changes of the n value correspond to a change of the elastic modulus for cortical bone in the range of 1075—600 kp/mm

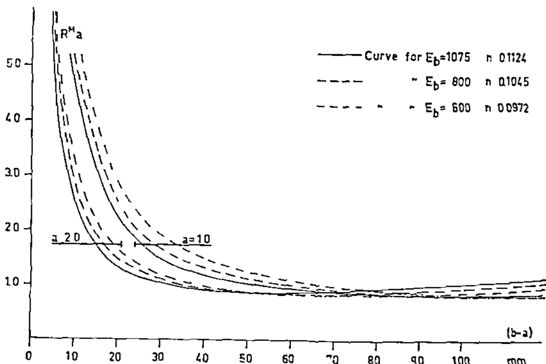


Fig 16 Edge deflection as a function of bone layer thickness and distance between the layers for three different values of modulus of elasticity of bone The two cortical layers are assumed to be of equal thickness and are designated *a* mm

Conclusions

From the tables and diagrams showing the quotients R^P and R^M the following special relationship can be derived

1 For each individual value of the distance between the cortical layers (b—a) the quotients become smaller with increasing cortical thickness This implies that areas with thick cortical layers should be singled out for nailing

2 As regards the influence of the forces it is found that with an increased distance (b—a) from 20 mm to the distance giving R^P minimum, an improvement of less than 5 per cent is obtained

The effect of the moment is altered however to a greater extent the thinner the cortical layer the greater is the change The percentage improvement that can be obtained by increasing the distance b—a from 20 mm to the distance which gives R^M minimum has been calculated in Table VII The conclusion can be drawn that the nail should be inserted in such a direction that a large distance is obtained between the cortical surfaces at least 20 mm The thinner the cortical layer the larger the distance must be

TABLE VII

Percentage improvement that can be obtained by increasing the distance $(b-a)$ from 20 mm to the distance which gives RM min. has been tabulated below as a function of the given parameters

Parameters	Cortical thickness mm	R^M min at $(b-a)$	Obtainable improvement $\frac{R^M - R^M_m}{R^M}$ per cent
$L_b = 1075$ $n = 0.1124$	$a = 1.0$ $a = 1.5$ $a = 2.0$ $a = 2.5$	90 60 50 37	60 50 34 24
$L_b = 800$ $= 0.1045$	$a = 1.0$ $a = 1.5$ $a = 2.0$ $a = 2.5$	105 75 55 50	68 [illegible]4 42 31
$L_b = 600$ $= 0.0972$	$a = 1.0$ 1.5 $= 2.0$ $a = 2.5$	120 85 65 58	74 60 50 39

Preliminary Experiments with Three Flanged Nail

A series of experiments was performed with the three flanged nail in order to find out the correlation between the theoretically calculated and the experimentally found values of the deflection of the edge and to determine the relation of the deflection to the nailing depth as carried into practice

The deflection of the edge was measured when the nail was subjected to bending stress inserted at different positions and depths into the acetabulum Furthermore experiments were carried out with the nail subjected to torsional stress The latter experiments were repeated with the nail driven through the femoral neck and head

The specimen consisting of half of the pelvis was attached to the stand described previously After preboring an Sv J nail was inserted into the desired direction and depth through the acetabulum

Through a bore of the acetabular edge a metal tube was fitted with its orifice placed next to the edge of the bone above the nail (Fig 17) A metal pin was introduced into the tube to contact the nail When the nail was loaded the movement occurring at the edge of the bone was transmitted by the metal pin The load was applied at right angles to the

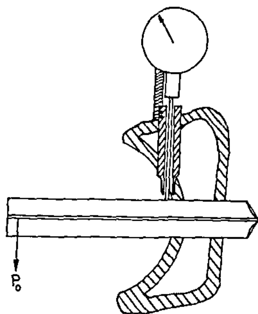


Fig 17 Experimental device for determining edge deflection caused by bending stress on three flanged nail Nail inserted through two cortical layers Dial indicator attached to bone

longitudinal axis of the nail The movement of the pin was read on a dial indicator The entire measuring device was attached to the bone and, consequently, the error in measurement due to the elasticity of the attachment device was eliminated Subsequently, the specimen was sawn through in the direction of the nail, so that the thickness of the cortical layers concerned and the length of the nail tunnel could be measured On the basis of these values, theoretical calculations were made on the direction coefficient of the deflection curve The latter was then put into relation to that measured at the experiment

The theoretically calculated and experimentally measured values of the direction coefficient of the deflection curve at varying nail depths and different cortical thicknesses are presented in Table VIII

The theoretical values of the direction coefficient are generally lower than the experimental ones The reason is that the bone material sometimes in practice deviates in a negative direction as compared to that of an ideal case accepted in theory

When hammering in the three-flanged nail small cortical fissures originating from the flanges regularly occur This means that the connecting factor of the bone material will be inferior around the nail In comparison with the ideal case as assumed in the theoretical analysis the deviation will be negative

TABLE VIII

Direction coefficient (K) of deflection curve
Experimental and theor tical values a b and L measured in mm

I_s 140 mm⁴ Test numb r	1	2	3	4
a	3 0	1 5	1 4	1,5
b – a	12	20	75	75
L – b	0 8	1 9	3 6	3 5
$K_{measured}$	3 0 10	4,28 10	2,85 10^{3}	2 10 10^{3}
K_{theor} (n = 0 1125)	0 95 10^{-}	1,27 10	0 89 10^{3}	0 87 10^{3}
K_{theor} (n = 0 0845)	2 80 10^{-}	3 83 10	2,28 10^{-3}	2 14 10^{3}

In cases where the nail penetrated a posterior cortical layer extensive fractures sometimes occurred This affected the securing and also had a negative effect on the measured values

For the theoretical calculations a fixed value which more or less can deviate from the value of the individual specimen was also applied to the modulus of elasticity

Temperature humidity loading speed and so on, are all factors affecting the elastic modulus (Sedlin 1965 Sedlin & Hirsch 1966 Hirsch & da Silva 1967) The conditions existing at the experiments may justify the use of values for elastic moduli which are in the lower *range of those* used for the theoretical calculations or even lower

The influence of various material factors can be represented in the mechanical model by a variation of the n value Table VIII shows the influence on the direction coefficient for a variation of the modulus of elasticity of cortical bone and of the elastic coupling *in the material* Thus the spring constant (C = k Eb) varies in the range of 600—1880 kp/mm² All these factors are included in the parameter n

The parameters n and Is (the moment of *inertia of the nail)* are essential for the values of the coefficient of direction Thus n is found in the second and the third potency through which even small changes will have a comparatively large effect on the result

Fig 18 presents the deflection of edge at various depths of nail insertion The nail has been directed *towards* the body of the iliac bone and its point has not penetrated any part of the internal cortex The diagrams show that the deflection of edge becomes much improved when the nailing

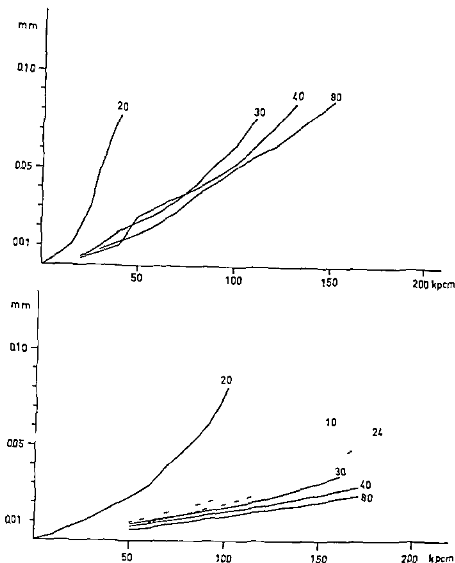


Fig 18 Edge deflection caused by bending stress on three flanged nail — — — — — — through two cortical layers ———— into body of iliac bone Figures on curves designate nailing depth in mm

depth is increased from 20 to 30 mm A nailing depth exceeding 40 mm will only give slight improvement

Experiments with Torsion Load

Experimental Device

The forces to which the nail has the least resistance act around the longitudinal axis of the nail

A special torque transmission device was designed (Fig 19) in order to find out the relation between nailing depth and deflection caused by torque

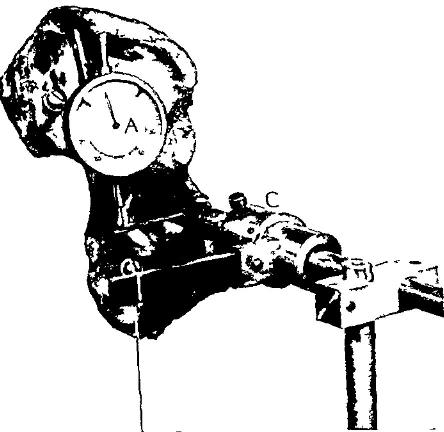
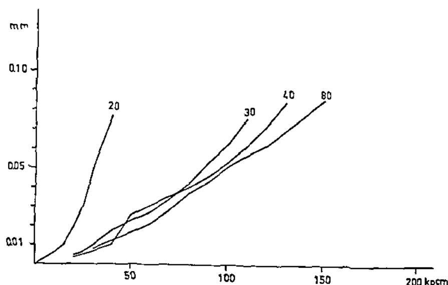


Fig 19 Experimental device for determining deflection caused by torque on three flanged nail A = dial indicator B = lever pin transmitting movement to dial C = torque transmission device D = loading lever arm

The device consists of a shaft at one end mounted with a sleeve by means of a ball bearing For transmitting the torque to the nail three screws are fitted in the sleeve A lever is welded to the sleeve

The three flanged nail was hammered into the desired depth of the mounted specimen The sleeve of the torque transmission device was slipped over the head of the nail and their longitudinal axes were centered to each other The shaft of the torque transmission device was fitted to the iron stand to prevent any bending moments The screws in the sleeve head were tightened to grip the space between the flanges of the nail



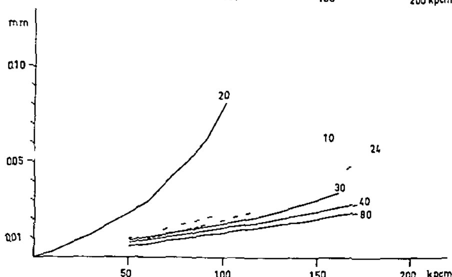


Fig 18 Edge deflection caused by bending stress on three flanged nail — — — — — — — through two cortical layers ————— into body of iliac bone Figures on curves designate nailing depth in mm

depth is increased from 20 to 30 mm A nailing depth exceeding 40 mm *will only give slight improvement*

Experiments with Torsion Load

Experimental Device

The forces to which the nail has the least resistance act around the longitudinal axis of the nail

A special torque transmission device was designed (Fig 19) in order to find out the relation between nailing depth and deflection caused by torque

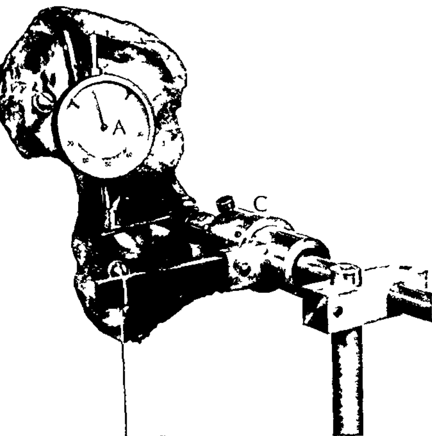


Fig 19 Experimental device for determining deflection caused by torque on three flanged nail A = dial indicator B = lever pin transmitting movement to dial C = torque transmission device D = loading lever arm

The device consists of a shaft at one end mounted with a sleeve by means of a ball bearing For transmitting the torque to the nail three screws are fitted in the sleeve A lever is welded to the sleeve

The three flanged nail was hammered into the desired depth of the mounted specimen The sleeve of the torque transmission device was slipped over the head of the nail and their longitudinal axes were centered to each other The shaft of the torque transmission device was fitted to the iron stand to prevent any bending moments The screws in the sleeve head were tightened to grip the space between the flanges of the nail

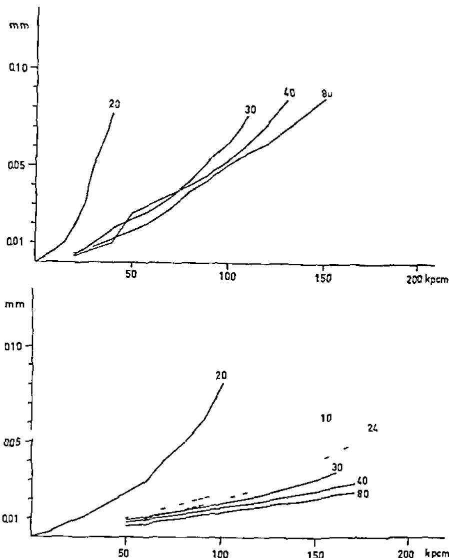


Fig 18 Edge deflection caused by bending stress on three flanged nail — — — — — — through two cortical layers ———————— into body of iliac bone Figures on curves designate nailing depth in mm

depth is increased from 20 to 30 mm A nailing depth exceeding 40 mm will only give slight improvement

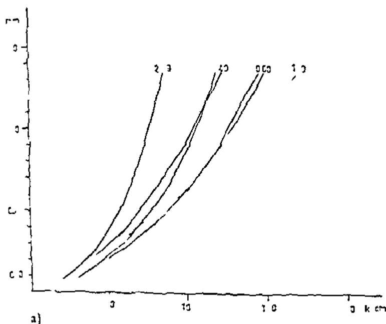
Experiments with Torsion Load

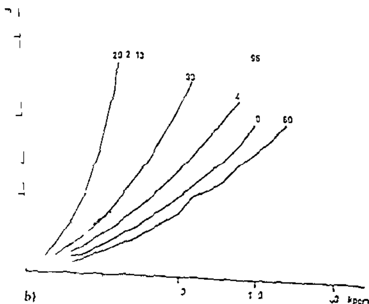
Experimental Device

The forces to which the nail has the least resistance act around the longitudinal axis of the nail

A special torque transmission device was designed (Fig 19) in order to find out the relation between nailing depth and deflection caused by torque

Fig 20 a b c Edge deflection caused by torque on three flanged nail — — — — — through two cortical layers ———————— into body of iliac bone — — — — — — — through femoral neck and head Figures on curves designate nailing depth in mm





The specimen was placed so that the nail and the longitudinal axis of the torque transmission device lay horizontally The lever of the torque transmission device was adjusted to lie horizontally as well By loading the lever, a gradually increasing torque was applied

A small metal lever pin was attached to the nail perpendicularly and also placed horizontally at a fixed distance from the acetabular surface A dial indicator was attached to the specimen by a metal rod so that its measuring point rested at right angles to the lever pin By attaching the dial indicator to the specimen it was possible to evade potential errors in measurement caused by movements in the attachment of the specimen

The dial indicator registered the movements of the lever pin in a tangential direction The lever pin thus described a circular movement while the dial indicator recorded changes in the set direction Thus, a systematical error in measurement was introduced which, however with respect to the effective range was considered to be of a negligeable magnitude

The lever arm also described a circular movement This error in measurement is also systematical and can be neglected in the utilized effective range The effect caused by the circular movements of the loading arm and the lever pin furthermore will counterbalance each other

The distance between the attachment of the lever pin on the nail and the acetabular surface was measured For measurement of the true torsion in the acetabular surface allowance must then be made for the torsion of the nail between the acetabular surface and the lever

Measurement of Torsion of Nail

For determining the natural torsion of the nail the described torque transmission device was used One end of the nail was fixed to a screw vice, and the other end to the torque transmission device Two points of the nail were fitted with levers which each affected their dial indicator A gradually increasing torque was applied and each indicator read The natural torsion of the nail was thus determined to 14 ,16 per 0 1 kpm and per 10 mm of the nail With satisfying accuracy the correction value 14 per 0 1 kpm and per 10 mm of the nail was used

Torsion Experiments in Acetabulum

The described method was used for a series of experiments In conformity with the bending stress there was a pronounced reduction of deflection of the edge when the nailing depth exceeded 20 mm The value is however slightly higher in connection with torque as compared to bending stress In reality a nailing depth of 4—5 cm should be attempted

continued using a three flanged die At the insertion of the nail the caput rested in a hemispherical metal cup or else in the acetabulum which thus offered adequate resistance Despite this fractures of the cortical surfaces were regularly noted The torque was applied to the nail from the caput side

Curves of deflection are marked in the diagrams which were obtained at the experiments of the pelvis The curves show that the resistance is about the same as for the greater depth on the pelvic side

Conclusions

The theoretical analysis and the experiments performed show that if a single nail is selected as an osteosynthetic technique certain points should be carefully considered As regards the nail it should have a great moment of inertia and shape properties which will give a minimum of fissures when penetrating the material This also implies that the cortical layer must not be fractured when penetrated As regards the edge deflection the nailing depth should theoretically amount to a minimum of 22 mm The cortical layers should be as thick as possible

The experiments have shown that there is a limit value for the nailing depth which exceeds 30 mm for bending stress and slightly higher for torsinal stress Thus the nailing depth should be at least 40 mm The securing will then not be less than that on the femoral side

This demand in reality means that only one direction of nailing is possible i e when the nail reaches into the body of the iliac bone Only then can sufficient depth be achieved Furthermore in this direction a suitably dimensioned nail will be fixed between two cortical layers This means that to the greater part it will rest in bone with cortical resistance properties Finally with this direction there is no risk of fractures in the internal cortical layer

Traumatic Effect of Three Flanged Nail

Nailing with a three flanged nail has revealed that there are great risks of fracturing the caput The nailing has been done carefully to cause as small a trauma as possible The caput rested in the acetabulum the preboring was done with great care and the nail tunnel was prepared with a die

With the nail well centered into the collum and the caput the risk of fractures seemed small provided that the tip did not reach or penetrate the cortex of the caput If this occurred fractures would regularly originate from the edges of the flanges If the nail went obliquely through the caput the risk of fractures increased This type of fracture usually appears as a

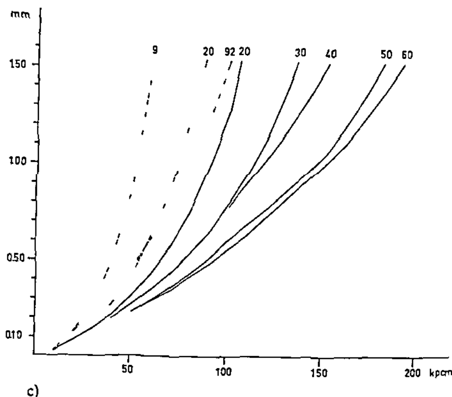


Fig 20 presents examples of deflection curves obtained at these experiments

The diagrams also include curves which were obtained with the nail in positions where it penetrated the posterior cortex The thickness of bone then varied from 9 to 24 mm The curves are at the same level as the one showing a nailing depth of 20 mm Thus penetration of the posterior cortex does not necessarily mean improvement of the stabilization This presents an uncertain factor depending on how the cortical surface is fractured when introducing the nail

Torsion Experiments in Neck and Head of Femur

The method described was also used for torsion experiments with the nail, introduced just below the greater trochanter up through the femoral neck and head The nail was inserted between 90 and 105 mm through the bone

The nail tunnel was carefully prepared before inserting the nail First a bore was drilled corresponding to the core of the nail The preparation

These fractures are not visible on the radiographs partly because they are concealed by the opacity of the nail partly because they are not superimposed on normal radiographs

Arthrodesis with Three Flanged Nail

Arthrodesis was carried out in 35 specimens using the three flanged nail for the osteosynthesis In five cases no measuring values could be obtained for statistical analysis because of undue complications with the specimens

The preliminary experiments and the theoretical analysis of the three flanged nail reinforcement suggested a minimum nailing depth of 30 mm and a desired nailing depth of 40 mm For the sake of relating these results to measurings on completed arthrodeses a series of 7 specimens was tested in which the nailing depth was less than 30 mm (Mean nailing d pth 24 4 ±3 9 mm) In the further experiments the nailing depth was at least 30 mm with a mean depth of 44 mm (±10 4 mm)

When comparing these two depths the result is inferior with the more shallow depth the mean value for the deflection being considerably higher as also the mean rank (Tables XI and XII)

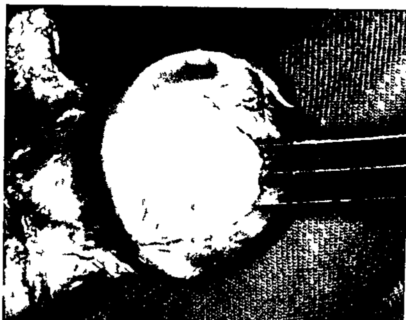
This confirms the results of the preliminary experiments

For the comparative experiments the greater nailing depth was used except for specimen No 75 which accordingly was excluded from the statistical analysis of the series

In using the sign test the values are significantly inferior for all the loading directions as compared to three point fixation with N nails The mean values of deflection are higher than for three point fixation and in ranking the mean rank places the method in a middle group (Tables X XI and XII)

In order to find out if any loading direction was inferior as compared to the others the four loading directions within each specimen and on levels *6 8 and 10 kp* were subjected to ranking (Table IX) Loading in extension gives the highest total ranking sum while the other loading directions are about equal In placing the loading directions in pairs according to the plane at which the movement takes place i e the frontal and the sagittal planes the fixation preventing movements in the sagittal plane will be inferior (flexion extension) The movement will then act about an axis which will coincide with the longitudinal axis of the nail In the minimum nailing depths (<30 mm) however the movements of the individual specimens in abduction and adduction often appear to be greater than in flexion extension

In order to reach into the body of the iliac bone which is necessary to obtain the desired nailing depth the nail must be inserted 2—3 cm



a

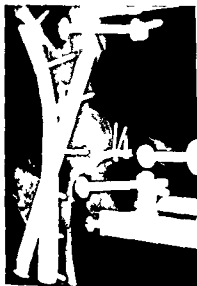


b

Fig 21 Traumatic effect of three flanged nail on femoral head
a) Detachment of triangular fragment
b) Fissure

fissure in the caput from a flange of the nail towards the periphery or else as a released and elevated triangular bone fragment This may happen even if the nail has not penetrated the cortex The tendency is more pronounced in a caput of a sclerotic type (Fig 21)

Fig 22 Radiographs of various types of tested appliances



a) 3 flanged nail and plate



b) Experimental nail + Nystrom nail



lpt N trom n 1 Frontal view



d) Oblique iew

TABLE IX

Sum of ranks of the four directions of loading at the Sv J nail

Kp	Flx	Abd	Ext	Add
6	49	46	74	51
8	46	45 5	73	55 5
10	50	45	71	54

below the greater trochanter, close to the anterior side of the femur at an angle of between 140 and 150 degrees (mean value 146° ±4 6) The nail penetrates the posterior upper lateral quadrant of the femoral head Thus, it will pass the longitudinal axis of the femoral neck under an acute angle both in the frontal and the transversal planes As a rule, it will lie very close to the posterior cortex of the neck, near the caput, which often *results in longitudinal fractures*

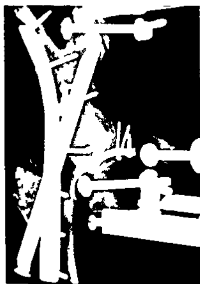
The described position of the nail implies a slightly flexed position of the arthrodesis, a mean position between abduction and adduction and also a mean position for rotation If the hip is flexed more, the insertion of the nail can be less anterior In abduction and outward rotation there is an increased risk of the nail not running all the way through the bone of the collum-caput From the point of view of nail position, *the ideal position for arthrodesis is flexion, inward rotation and adduction* The nail will then lie optimally centered in the bone From the clinical point of view, this is an impossible position

Three-Flanged Nail and Plate

Osteosynthesis with nail and plate was performed according to Alvik (1961) (Fig 22 a) The difficulty with the method is to obtain a good fit and satisfactory contact of the plate to the bone *The plate should cover* the part from the ilium across the joint to the front side of the proximal femur It is attached to the bone with several screws A comparatively good fit of the plate is obtained by bending it properly This may, increase the risk of corrosion (Venable & Stuck 1948)

This technique was tried on 8 specimens A comparison has been made with the three-point fixation with the three-flanged nail only and, finally, with a three flanged nail together with a lateral medial inserted N nail In the sign test the three-flanged nail and plate showed significantly reduced movement for flexion extension as compared with both the three point fixation and the simple three flanged nail (Table X) On the other hand, there was no significant *difference between these methods as regards* mobility with load in the abduction-adduction direction As compared with the three-flanged nail and an N nail there was no significant differ

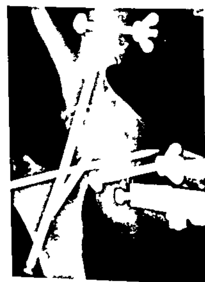
Fig 22 Radiographs of various types of tested appliances



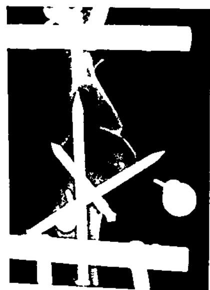
) 3 flanged nail and plate



b) Experimental nail + Nystrom nail



) 3pf x Ny trom na ls Fr ntal view



d) Obl que view

TABLE IX

Sum of ranks of the four directions of loading at the Sv J nail

Kp	Flx	Abd	Ext	Add
6	49	46	74	51
8	46	45 5	73	55 5
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i) Jpfix screws



j) AO compression plate

ence in flexion and adduction In abduction loading there was greater mobility while in extension loading the mobility was reduced The mean values of deflection in 6 8 and 10 kp were low (Table XI) In analysis ranking placed the method in the best group with respect to stability (Table XII) Thus it offers good stability but the application is rather difficult

Three Flanged Nail and N nail

The experiments with the three-flanged nail resulted in great mobility when loading in the flexion extension direction The three-flanged nail will only have one point of fixation The special shape of the cross section improves the resistance to bending and torsion stress as compared to a circular shape Despite this the fixation with the three flanged nail could perhaps be improved by fixing an additional point in the contact surface between the caput and the acetabulum This point should then be at a distance as far as possible from the three flanged nail Thus the specific load in the bores will be reduced and more so the play in the acting point of the force actually the movement between the surfaces will decrease (Fig 23)

On the basis of the shape of the pelvis there are consequently two possible positions for the complementary nail viz positions II and III (Fig 24)



e) Axer nail



f) Fox nail



g) Niebauer nail



h) Mc Kee lag screw

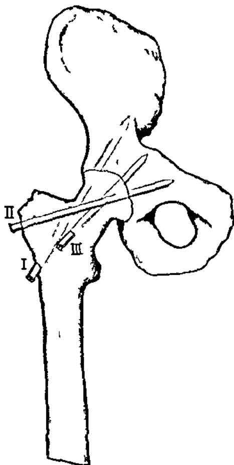


Fig 24 I II III show the respective positions of nail referred to in text

an N nail inserted from the greater trochanter and transversally directed into the acetabular part of the pubic bone the stabilization was considerably improved The clinical procedure is also simple due to television roentgen and does not magnify the incision

Three Point Fixation with Nails

In an earlier investigation (Graziati & Kalén 1965 Kalen 1965) a better result of stabilization was reported for arthrodesis of the hip by employing three thin nails of the N type as compared to fixation with a three-flanged nail The N nail type was found to be superior to the three point fixa

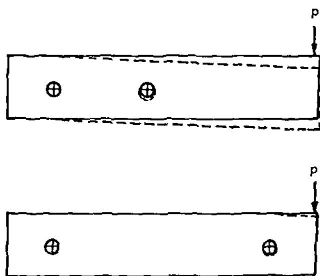


Fig 23 Deflection in short and long distances between points of fixation

The dimensions of the upper femoral end and of the three flanged nail prevent the use of a complementary nail of the same dimensions The large moment of inertia of the three flanged nail also makes this unnecessary Instead a nail of a thinner dimension is selected which can easily be placed inside the bone without affecting the large three-flanged nail The two nails will penetrate the proximal femur about 10 cm This will cause the nails to be well connected to each other There is no additional advantage in letting the thinner nail run through a hole in the coarser one, as in Witt s double nail A disadvantage with this arrangement is that the direction of the thin nail is set Consequently it may be impossible to select a position which will give the best securing on the pelvic side

Using an N nail in positions II and III a series of comparative experiments was carried out to establish the most suitable position for the nail These experiments were made on 4 specimens An N nail placed in position II (lateral medial position) gave a significantly better result than a nail in position III (main direction anterio posterial) (Table X) The first position was selected for the subsequent experiments

The technique was tried in a total number of 12 specimens In comparison with the three point fixation there is no significant difference in any loading direction As opposed to this there are significantly better values in all the loading directions as compared with the simple three flanged nail (Table X) In ranking this technique was placed in the best group from the point of view of stability with a mean rank below 4 (Table XII)

Thus it was found that simply by completing a three-flanged nail with

When compiling the experiments with the sign test a significantly im proved fixation is found for all the load directions as compared to fixation with a three-flanged nail (Table X) The same result is found in comparison with three-point fixation with screws and with compression techniques As compared to a three-flanged nail plus a lateral medial directed N nail there is no significant difference In comparison with a three flanged nail and plate there is no significant difference in the load directions adduc tion abduction but negatively in flexion extension

When compiling the method with the descriptive calculations there are low mean values for the deflection at 6 8 and 10 kp The ranking places the method in the best group with a mean rank of 3 50 (Tables XI XII)

Variations of Three Points Fixation with Nails

Osteosynthesis with three nails was varied by substituting the N nail in position I for a nail of a larger dimension An N nail of a 6 mm dimen sion was tested and also a triangular nail in principle a three flanged nail without flanges the latter having a maximum diameter of 8 mm

On comparison between the different types of nail and the conventional ones used for fixation there is a significant difference in favour of a nail of the latter type in position I However no significant difference could be found when the usual N nail in position I was replaced by a slightly coarser nail of the same type

It should be pointed out that the coarser nails were inserted into the same tunnel as the thin N nail first introduced and then the specimen was re-tested This will impair the conditions of the latter nails which to a certain extent explains the indemonstrable difference between the N nail of 4 and 6 mm dimensions

Three Point Fixation with Screws

Osteosynthesis was performed according to Merle d Aubigne (1964) with the nails in the positions recommended by him The length of the screws was between 12 and 14 cm The root diameter was 3 6 mm and the dia meter over the threads 6 mm The technique was carried out on ten spe imens as comparative experiments (Fig 22 i)

This technique was always performed first in order to *ensure the best* conditions for the screws As a second technique the three point fixation with nails was performed The results show significantly inferior values for the fixation with three screws in all loading directions The descriptive calculations show a mean rank sum which ranges within higher values (Tables X XII)

tion with Steimann pins The difference can be explained by the circular cross section of the latter type

The aim with fixation of this type is that each nail should lock the movement which occurs in a plane perpendicular to the longitudinal axis of the nail The ideal is to place, if possible the nails at an angle of 90 degrees The maximum distance between each point of fixation in the spherical surface between the caput and the acetabulum is then obtained *The anatomical conditions are of a kind that the parts of the pelvis* which offer the greatest nailing depth are placed so that their longitudinal axes will intersect each other at an angle of less than 90 degrees On the femoral side, two of these directions will allow the nail to be inserted into the bone at a depth of between 8 and 10 cm, the third alternative of no less than 6 cm (Figs 24 6)

The outlined technique is in good accordance with the technological principle which expresses that for stabilization of a piece of material the *points of fixation should be placed as far from each other as possible*

The thin nails of the N type have a diameter of 4 mm with a square cross section and slightly concave sides Due to this dimension, a very *small portion of the bone material is involved, and the technique has* therefore been considered suitable to use as a reference method when evaluating the other techniques of osteosynthesis

The position of the nails in three-point fixation is as follows one nail is placed in the same position as for fixation with a three flanged nail, i e into the body of the iliac bone (No I, Fig 24) A second nail is directed from the posterior part of the greater trochanter transversally and medially into the acetabular part of the pubic bone (No II) The third nail is intro *duced slightly below the centre of and inside, the intertrochanteric line* It takes a posterior course slightly medial and cranial into the spine of the ischium (No III)

At the experimentally performed arthrodesis the insertion of *nails in* the described directions does not involve any difficulties The small dimen sions of the nails and their position will prevent them from contacting each other

In clinical surgery there is no difficulty in placing nails Nos I and II Instead nail No III which is directed to the spina of the ischium may involve a certain risk of nerve and vascular injury if the tip is uncontroll ably hammered through the cortex of this area

When introducing the nails into the femur the cortex has always been prebored with a suitably dimensioned drill This is essential in positions I and III as these nails penetrate the cortex under an acute angle The cortical layer into which nail No I is inserted is furthermore rather dense

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Compression Nail according to Fox

The osteosynthetic material consists of a nail with a square cross section and concave sides The tip is designed to cause gradual scooping of the nail tunnel There is also a locking washer to secure the tip of the nail inside the pelvis It is coarser of a more simple design and easier to apply than the Axer nail In this technique a plate is also fitted across the head of the nail The plate is fixed to the femoral shaft with through screws When the end nut is tightened the compression is transmitted via this plate to the femoral portion No helical spring is used (Figs 22 f 25 b)

The method has been tested on 6 specimens all comparative experiments with three point fixation

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Compression Nail according to Niebauer

The nail is three-flanged and has a slightly coarser dimension than the Axer nail The locking washer on the inside of the pelvis also differs The compression is brought about with a nut via a sleeve mounted on the head of the nail (Figs 22 g 25 c)

The method was only tested in 3 specimens In one of these the stabilization only allowed a load of 4 kp in two directions The stabilizing effect is clearly inferior as compared to the three-point fixation Niebauer also recommends a complementary screw from the upper edge of the acetabulum through the caput in a caudal direction The technique at present does not seem to be in clinical practice

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The load and muscular force, always cause compression As the technique with nails gives better stabilization and is easy to apply, there is actually no reason to use screws instead

Compression Methods

Four different methods for osteosynthesis with compression have been tried In three of these, viz the methods according to Axer, Fox and Niebauer the same procedure, in principle is utilized

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The fourth method according to Mac Kee consists of a coarse screw which is inserted into the acetabular roof

These methods have been tried on a total of 23 specimens The cartilage was carefully removed from the joint surfaces involved as when employing the methods of compression, an increased friction between the surfaces could be of importance for the efficiency of the fixation

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With osteosynthesis of this type there is a risk that the threads of the pin may catch in the plate which rests against the femoral cortex It is necessary to take care that this does not happen as otherwise the compression in the arthrodesis will not be that intended

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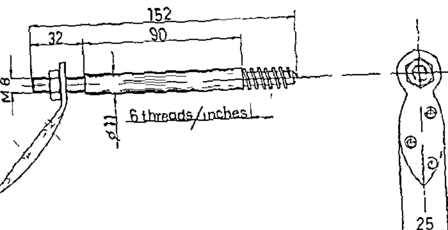
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d) Compression screw according to Mc Kee

Fig 25 a—d Construction drawings of tested compression devices The measurements are expressed in millimeters

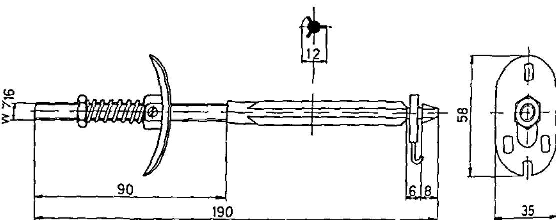
Compression Screw according to Mac Kee

The screw is inserted through the collum/caput and screwed into the acetabular roof reaching a depth of 2 5 cm Only the part on the acetabular side is threaded with wide threads while the part of the screw in the femoral portion is smooth cylindrical Also here there will be compres sion by means of a nut fitted on to the threaded outer end of the nail

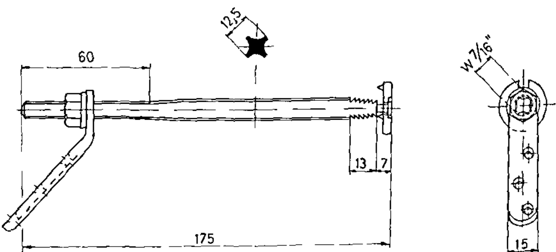
The method was tried in 6 cases as comparative experiments to the three point fixation Two of these however had to be excluded as suf ficient fixation for minimum loads could not be obtained Only in one case were all four loading directions recorded with 4 6 and 8 kp respec tively (Figs 22 h 25 d)

At the sign test the values of deflection were significantly higher as compared with the three-point fixation (Table X) The mean values obtain able for the deflection were high (Table XI) Due to the low number of ob-servation ranking could not be calculated for loads of 6 8 and 10 kp As the stabilization in the e experiments was poor there was no reason to in crease the series The poor stabilization depended on insufficient securing to the acetabulum a short portion of the screw inserted into spongy bone and on the circular section of the screw The first condition is the reason for an inferior preventive effect of the movement in abduction and adduc tion loading the latter refers to the flexion extension loading

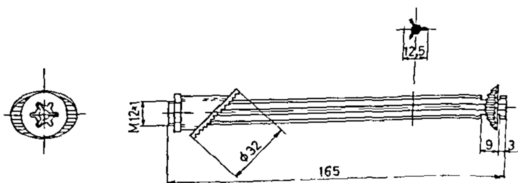
In loading where the movement will occur close to the longitudinal axis of the screw i e mainly flexion extension, the counteracting force will only



a) Compression nail according to Axer



b) Compression nail according to Fox



c) Compression nail according to Niebauer

TABLE X

Result of Sign test

	3pfix N	3pfix N mod	Sv J	Sv J +N position II	3pfix screws
3pfix N mod	0 0 0 0				
S J	+ + + +				
3pfix (S J mod)	0 – – –				– – – –
3pfi scr ws	+ + + +	+ + + +			
Sv J + N position II	0 0 0 0		– – – –		
Sv J + N posit on III				+ + + +	
Sv J + plate	– 0 0 –		– 0 0 –	0 + 0 –	
Axe nail				+ + + +	
Fo na l	+ + + +				
Mc Ke sc ew	+ + + +				

\+ means that the line method gives signif cantly higher values of S than the column method

— means that the l ne method g ves s gnificantly lower values of S_m than the column method

0 me ns that the e is no sign ficant diffe ence

A rega ds the load n direct ons the si n are set as follows

Flex on Abd tion

Extens on Adduct on

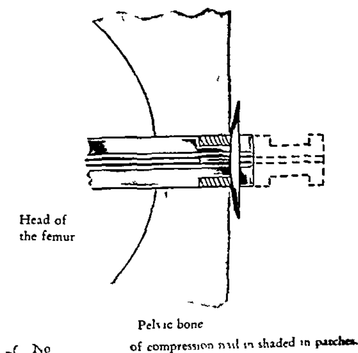
radius This means that the force intended to be transmitted between these surfaces will be concentrated within a rather small area around the nail

The position of the nail means that the longitudinal axis will lie close to that of the collum Loading in flexion and extension will then mainly appear as torsion stress From the femoral side it will be transmitted to the pelvic side partly by friction between the joint surfaces partly via the

be the friction force between the joint surface (primarily increased through compression) and friction between the screw threads and the bone in the acetabulum

Summary

In summary none of the tested methods of compression with nail or screw offered stabilization to a degree which could be expected Stabilization with compression should theoretically give a better result than without The reason of this not being the case may depend on the quality of the utilized bone on the pelvic side The average thickness of the bone layer penetrated on the pelvic side was for the Axer nail 17 mm with a variation ranging between 11 and 25 mm and for the Fox nail 16 mm with a variation between 11 and 20 mm As the nails in a small area inside the locking plate lack flanges a few additional millimeters are lost because the nail is pulled back at the compression (Fig 26) The cortical layer of the pelvis is thin within the area concerned and not of the quality which for instance is found on the femoral side where the nail is inserted Thus the bone cannot always resist the great stress concentration which will occur Especially the curved locking plate used for the Niebauer nail causes impression in the underlying bone when subjected to compression It should also be pointed out that *the joint surfaces around the nail which are compressed* against each other are not plane but spherical with a sometimes varying



-f No of compression nail in shaded in patches.

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Result of Sign test

	3pfix N	3pfix N mod	Sv J	Sv J + N position II	3pfix screws
3pfix N mod	0 0 0 0				
Sv J	+ + + +				
3pfix (Sv J mod)	0 — — —				— — — —
3pfix screws	+ + + +	+ + + +			
Sv J + N position II	0 0 0 0		— — — —		
S J + N position III				+ + + +	
Sv J + plate	— 0 0 —		— 0 0 —	0 + 0 —	
A er n l				+ + + +	
Fox nail	+ + + +				
McKee screw	+ + + +				

\+ means that the line method gives significantly higher values of S_m than the column method

— means that the line method gives significantly lower values of S than the column method

0 means that there is no significant difference

As regards the loading directions the signs are set as follows
Flexion Abduction
Extension Adduction

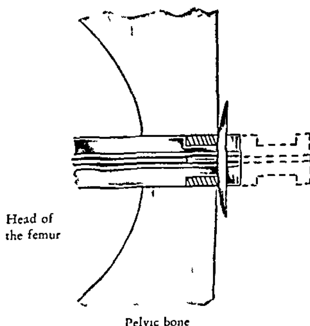
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Figs 26 No bone contact of compression nail in shaded in patches

Sv J + plate

Loading kp	Flx	Abd	Add	Ext	No of obs
6	6 25	12 63	25 00	6.25	(8 8 8 8)
8	11 63	20 50	35 75	10 00	(8 8 8 8)
10	16.38	31 13	23 14	14 50	(8 8 7 8)

Exp nail + N (position II)

Loading kp	Flx	Abd	Add	Ext	No of obs
6	7 5	6 5	6.3	10 1	(10 10 10 10)
8	13 1	10 7	10 9	14 6	(10 10 10 10)
10	16 9	14 9	15 9	20 3	(10 10 10 10)

Fox N il

Loading kp	Flx	Abd	Add	Ext	No of obs
6	21 83	26 83	26.33	26.33	(6 6 6 5)
8	33 80	46 67	27 20	49 00	(5 6 5 5)
10	38 75	34 67	40 40	52 50	(4 3 5 2)

Axer Nail

Loading kp	Flx	Abd	Add	Ext	No of obs
6	68.25	123 25	129 28	121.37	(8 8 7 8)
8	73 83	99.33	140 50	125.33	(6 6 6 6)
10	111.25	138 40	115 40	158 00	(4 5 5 5)

Mc Kee screw

Load ng kp	Flx	Abd	Add	Ext	No of obs
6	80 75	107.33	185 00	100 75	(4 3 3 4)
8	47 00	–	–	–	(3 –)

TABLE XII

Ranks of methods

Meth od	Sum of ranks ov d rect ons			Sum of ranks over loadings				Total sum of ranks	Mean r nk
	6 kp	8 kp	10 kp	Flx	Abd	Add	Ext		
3pfi N	10	13	19	13	8	9	12	42	3 50
3pfi N mod	24	27	27	21	22	16	19	78	6 50
3pfi S J mod	6	5	5	4	3	3	[illegible]	16	1.33
3pfix sc ew	40	36	39	29	28	30	28	115	9 58
S J > 30 mm	29	29	32	24	17	24	25	90	7 50
S J 30 mm	44	47	45	34	35	33	34	136	11.33
Sv J N pos II	16 5	14	17	11 5	9	15	12	47.5	3 96
S J N pos III	18 5	21	18	13 5	18	14	12	57 5	4 79
S J plat	14	16	12	5	14	20	3	42	3.50
A na l	48	45	47	35	34	[illegible]	35	140	11 67
I na l	34	[illegible]	35	28	25	24	28	105	8 75

TABLE XI

Mean values for S_{ma}

3pfix N

Loading kp	Flx	Abd	Add	Ext	No of obs
6	9 94	6 28	10 80	15 83	(49 50 49 50)
8	14 92	12 36	18 65	23 68	(49 50 49 50)
10	21 32	20 37	26 75	29 94	(47 49 49 47)

3pfix N mod

Loading kp	Flx	Abd	Add	Ext	No of obs
6	12 77	14 77	16 44	20 44	(9 9 9 9)
8	20 66	24 88	26 55	29 22	(9 9 9 9)
10	24 00	36 43	32 00	39 86	(7 7 7 7)

3pfix (Sv J mod)

Loading kp	Flx	Abd	Add	Ext	No of obs
6	7 17	2 50	4 50	8 83	(6 6 6 6)
8	11 33	4 33	6 33	12 83	(6 6 6 6)
10	15 83	6 17	8 33	18 50	(6 6 6 6)

3pfix screws

Loading kp	Flx	Abd	Add	Ext	No of obs
6	30 89	36 89	27 44	38 20	(9 9 9 10)
8	31 14	30 71	42 00	41 75	(7 7 7 8)
10	46 50	46 67	71 50	52 28	((6 6 7)

Sv J (Depth of insertion > 30 mm)

Loading kp	Flx	Abd	Add	Ext	No of obs
6	20 89	13 47	22 84	26 47	(19 19 19 19)
8	24 61	21 68	34 05	40 63	(18 19 19 11)
10	26 87	32 58	45 16	44 50	(16 18 19 16)

Sv J (Depth of insertion < 30 mm)

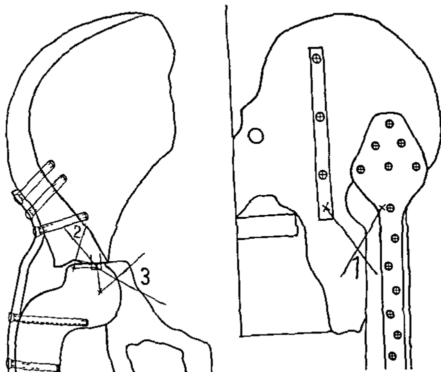
Loading kp	Flx	Abd	Add	Ext	No of obs
6	41 86	66 67	93 25	112 20	(7 6 4 5)
8	77 00	113 50	92 67	132 00	(7 6 3 4)
10	63 20	167 00	105 67	101 00	(5 4 3 3)

Sv J + N (position II)

Loading kp	Flx	Abd	Add	Ext	No of obs
6	11 25	9 25	14 92	17 25	(12 12 12 12)
8	13 36	16 67	23 17	24 25	(11 12 12 12)
10	18 36	19 40	32 40	21 00	(11 10 10 10)

Sv J + N (position *III*)

Loading kp	Flx	Abd	Add	Ext	No of obs
6	11 25	16 25	14 50	17 00	(4 4 4 4)
8	17 75	24 50	23 00	25 50	(4 4 4 4)
10	17 33	21 00	32 75	20 00	(3 3 4 3)



F 27 Posit on of displacement gauges when testing AO compression plate

does not always allow the plate at the attachment to the ilium to be fitted in close contact to he bone The bone to which it is screwed is of a thin dimension and has lower resistance properties than for instance the sturdy cortex of the femoral shaft De Palma (1962) complained of the difficulty in obtaining a satisfactory attachment for screws in this region and instead recommended through bolts The applied compression may partly compensate the inferior attachment but for example in abduction load the compression force will be reduced between the contact surfaces in general and in extension flexion load within certain areas

As regards the contact surfaces the ilium will after osteotomy offer a very narrow bone area for contact with the surface of the caput The caput will thus balance on this narrow bone surface when compression is applied The contact surface of the ilium can be increased by placing the osteotomy on a more proximal level but as this is done the contact sur face of the caput will be reduced accordingly

The bone surfaces which are to be compressed will also lie at a great distance from the plate which causes compression

Finally the osteotomy performed dorsally to the acetabulum will leave

flanges of the nail to the external cortical surface of the pelvis and its spongy bone Finally, the torsion stress may be transmitted via the stop plate to the internal cortex This is especially pronounced in using the Fox and Niebauer nails while, contrary to this, the locking plate in Axer s technique allows the nail to turn freely

In all the experiments these compression methods were inferior to the reference method In analysis the ranking procedure revealed that the compression methods do not offer better stabilization than an adequately fitted three flanged nail

Arthrodesis with Compression Fixation according to AO

Arthrodesis was performed by the use of the technique described by Muller in the AO-Bulletin September 1967 With this technique the osteotomy of the pelvis is made horizontally at the level of the upper acetabular edge and releasing a segment of the upper part of the caput The caput is displaced medially so that its planed upper surface will contact the bone surface of the ilium medial to the acetabulum Part of the greater trochanter is removed by saw and then a specially designed cross plate is screwed on to the outside of the ilium so that the plate will contact the proximal femoral end laterally Compression is applied by using AO s compression device and then screwing the plate to the femoral shaft (Fig 22 j)

As the caput and the acetabulum are not kept intact when this technique is used, the earlier measuring technique was not applicable Thus comparative experiments could not be executed either The measurings were performed with three measuring calipers, fitted according to Fig 27

Due to pelvic osteotomy the pelvis could not be fixed in the same way as in earlier experiments The ilium was instead fixed by means of polyester The osteosynthesis leaves the entire ischio pubic portion of the acetabulum unstabilized

Measurings were performed in three cases In all the cases there was a certain amount of mobility in all the four tested load directions The lowest reading was obtained for adduction load which was expected, as there will then be a force component in a direction which will increase the compression

Digrams, (Fig 28), exemplify the recorded movement in the three transducers with increasing load in the four tested load directions Thus a total movement as S_m is not reported as in earlier diagrams No relevant comparison with these values can consequently be made It has merely been established that the method will not give rigid fixation

Certain fixed factors may thus be involved The design of the plate

Besides a form factor the properties of the nail are determined by a material factor namely the physical properties Due to the demands made on the corrosive resistance the selection in reality is limited stainless steel vitallium titanium For the experimental nail stainless steel was selected

The moment of inertia of the nail completely depends on the form factor It is defined for the perpendicular cross between the axes as follows

Moment of inertia with respect to x axis $$I_x = \int_A y \quad dA$$

With respect to y axis $$I_y = \int_A x \quad dA$$

The designed nail will according to the dimensions in Fig 29 receive a moment of inertia amounting to 350 mm⁴ (compare the Sv J nail 140 mm⁴)

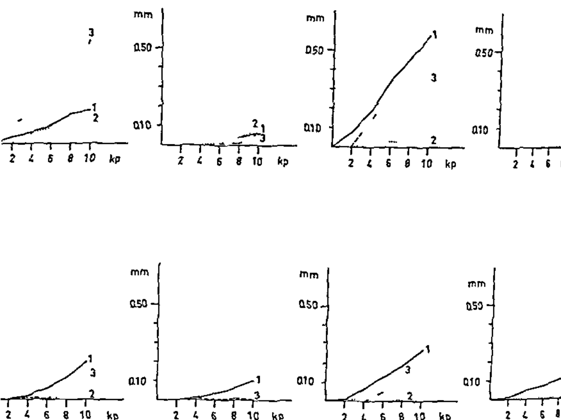
A cross section which gives a large moment of inertia in certain directions is the H form It has been utilized previously for nail designs by Frankel (1960) and Laing & O Donell (1961) This section however causes difficulties in shaping the tip as the aim is to create as small a nailing in resistance as possible Furthermore it may also involve a chiselling effect in the bone

To obtain equal resistance of the nail in various directions it is necessary that its properties be uniform and therefore the design should be quite symmetrical if possible The moment of inertia will then be constant in all the directions A four flanged section is consequently preferable The solid bone lying between the flanges will diminish by an increased number of flanges An optimal relation between the number of flanges and the dimensions of the intermediate bone area should be attempted

By finishing each flange with a circular segment instead of a pointed angle the moment of inertia will increase and at the same time the chipping effect will be reduced

Due to the shape of the bone in that particular area a nail dimensioned 12 mm was selected It is slightly smaller than the conventional Sv J nail

To reduce the risk of fissures occurring along the flanges of the nail at the insertion the tip of the nail also has a special design The nail has been extended from its middle to a circular tip in order to fit in a bore of the same dimension The tip of the flanges have been guided back in relation to each other so that they will each rest against the bone surface This means that a plane through the tips of the flanges will be at an angle of 145 degrees against the longitudinal axis of the nail This will prevent the nail from sliding along the cortical surface Furthermore the tip of each flange is shaped as a cross ground edge directed slightly towards the centre of



Figs 28 AO compression plate Experiments 109 and 112 The diagrams show displacement in gauges in positions according to Fig 27

large, open spongy bone surfaces which are not utilized for compression but clinically will be the source of extensive bleeding

Nail Design

The experiments which were performed on the basis of the theoretical analysis of the three-flanged nail show slightly higher values for the edge deflection than the theoretical values

The reason is mainly the impaired resistance resulting from the fractured bone connected with the insertion of the nail The properties of the nail furthermore, are also decisive for the result The moment of inertia of the nail is an important factor It should be as large as possible The dimensions of the nail should be such that it will remove as little as possible of the bone material Finally, the anatomical shape of the bone areas concerned is a factor to consider when dimensioning the nail

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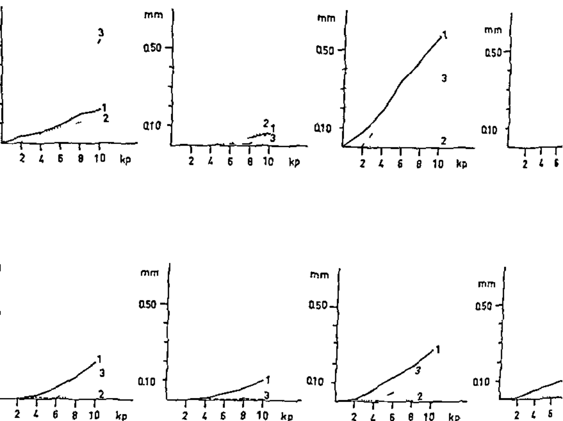
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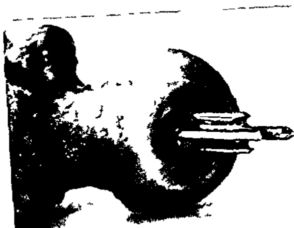
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a)



b)

F g 30 Expe me ıtal naıl a) note no trau natıc effect
b) after removal of naıl

(Compare Fıg 21)

In order to create as equal condıtıons as possıble ıt was decıded that each naıl would be tested on the rıght left sıdes of the same specımen Four of these experıments were performed It was found however that the spe cımen factor by no means was elımınated by thıs Furthermore there were

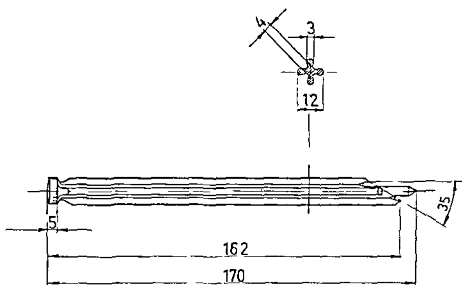


Fig 29 Construction drawing of experimental nail The measurements are expressed in mm

the nail When the nail is inserted, this edge will chisel out small fragments of bone Inside this edge at an angle of 90 degrees the flange itself is ground to an edge At the insertion small fragments of bone will be chiselled out and guided into the groove between the external coarser edge of the flanges and the centre of the nail They will accumulate here and definitely improve the securing of the nail

Testing of Experimental Nail

The earlier investigations showed that the three flanged nail combined with a thin transversal nail gave a very good primary fixation Thus there was no signficant difference as compared to the three-point fixation with thin nails The purpose of the new designed experimental nail was to replace it for the three-flanged nail used in this method of stabilization Bearing in mind the disadvantages of the three-flanged nail the efficiency of the nail joint should gain

So that any difference between the experimental nail and the three flanged nail could be determined in practice it would have been advantageous to compare measurements with both nails tested on the same specimen As both nails however do not differ much with respect to dimension, and the position of both nails should be in good accordance, an experiment of that type would not be just The nail tried first will actually give such a loss of bone substance that the securing conditions for the following nail will be very poor



a)



b)

Fig 30 Experimental nail a) note no traumatic effect
b) after removal of nail

(Compare Fig 21)

In order to create as equal conditions as possible it was decided that each nail would be tested on the right left sides of the same specimen Four of these experiments were performed It was found however that the specimen factor by no means was eliminated by this Furthermore there were

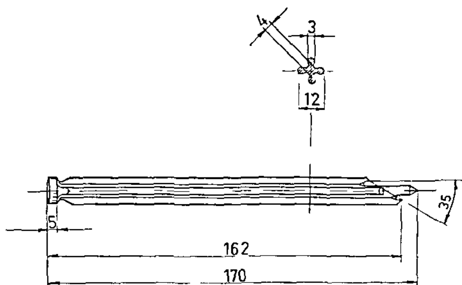


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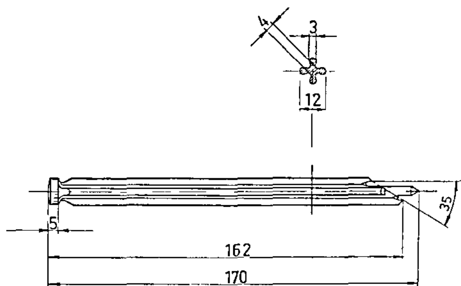


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TABLE XIII

Sign test 3pfix N — E + N (pos II)

Loading direction	Numbers of observations 3pfix N > E + N	Total number of observations	Significance
Flx	31	41	yes
Abd	18	41	no
Add	16	39	no
Ext	35	47	yes

difficulties in obtaining whole pelvic specimens to the required extent

As direct comparative experiments could not be carried out, a series was tested using the experimental nail with an N nail and with the three-point fixation as a reference method This *series includes ten specimens* On each specimen osteosynthesis was first done with three N nails Then the nails in positions I and II were removed (Fig 22 b), and the experimental nail was inserted into position I

In assessing the measured results and carrying out the sign test, there is a significantly greater mobility with three-point *fixation in loading in* flexion extension On the other hand, there is no significant difference between the tested methods in abduction adduction loading (Table XIII) The mean values for S_{max} are low, (Table XI) and ranking between certain methods places the method on the top (Table XIV)

In a test series with an Sv J-nail combined with a transversal nail and compared to three-point fixation, the sign test did not show any significant difference By testing against the same reference method, as used here an indirect comparison can be made As no direct comparative experiments were carried out the results cannot be regarded as statistically significant

The results obtained, however, support the opinion that the new designed nail gives a better result than that of the conventional three flanged nail

It can well be explained that an improvement is obtained in flexion extension in comparison with the three flanged nail but that no difference can be demonstrated in abduction adduction Loads in the latter directions *will cause considerable bending stress to the nail The moment of inertia* of the nail will be of great importance However the moment of inertia for both nails is satisfactory in the loads concerned When loading in flexion extension the nail will on the other hand transmit torsional stress Any fractures of the bone emerging from the flanges will result in an *impaired stability*

When performing arthrodesis it was established that the new designed nail had a reduced traumatic effect in the bone In no case was there any

TABLE XIV

Ranks of certain methods

Method	Flexion			Abduction			Adduction			Extension			Sum of ranks
	6kp	8kp	10kp	6kp	8kp	10kp	6kp	8kp	10kp	6kp	8kp	10kp	
E + N	1	1	1	2	1	1	1	1	1	1	1	1	13
3pfix N	2	2	2	1	2	2	2	2	2	2	2	2	23
Sv J	3	3	3	3	3	3	3	3	3	3	3	3	36
3pfix screws	4	4	4	4	4	4	4	4	4	4	4	4	48
Compress on nails and screw	5	5	5	5	5	5	5	5	5	5	5	5	60

fracture of the caput or the acetabulum which was comparable to that caused by the three flanged nail (Fig 30) Subjectively it also gave a clear impression of penetrating the bone easier This also means that the risk of diastasis developing in the joint when the nail is inserted will be reduced By inserting the transversal N nail first the risk is completely eliminated

Electro-Mechanic Hammer

During the course of the experiments it was found that a special tool for insertion of the nails would be of advantage The reason for this was to get a better control of the force of impact and an even distribution of the required energy It was hoped that by this the traumatic effect of the nail would be further reduced In co operation with the Division of Computer Research Chalmer s Institute of Technology, University of Goteborg an electro-mechanic hammer was thus designed and manu factured

The principle of the design is depicted in Fig 31 It consists of an electric coil inside which a core of soft iron slides One end of the core is spring-loaded When the coil receives an electric impulse, the soft iron core moves into the coil This results in force of impact The energy is transmitted to a hammering pin which is designed to grip the head of the nail The nail is fitted to the pin by means of a sleeve which can be ex changed to fit all the nail dimensions The sleeve is fitted to the front side of the hammer by means of a bayonet clutch

A pulse generator, powered from 220 V mains supplies the coil in the hammer with pulses of suitable frequency and energy The pulse energy and thus also the force of impact is via a semiconductor-controlled rectifier operated with a pedal The control unit is equipped with an illuminated main switch and a switch for the pulse frequency selector The selector can be adjusted to produce 12 5 or 6 25 strokes per second The hammer also has a switch to alter the force of impact one position for nailing and one on a lower level for chiselling

Within each position the force is controlled by means of the pedal The controlling devices with which the tool is equipped ensures a lenient and rapid insertion of the nail The tool can also be used for an effective and precise chiselling

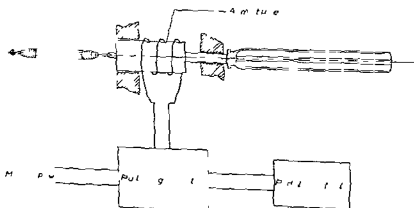


Fig. 31 Photo aph and principle sketch of elect o mechani hammer On the photo graph re seen the p l e gene ator the hammer d fferent sleeves nails and *chisel*

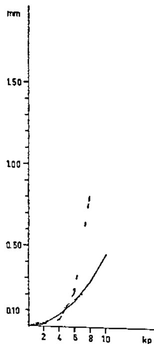
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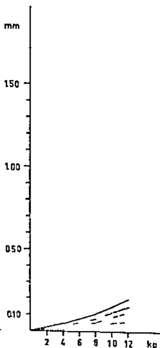
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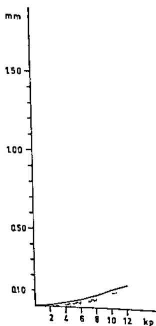


Fox

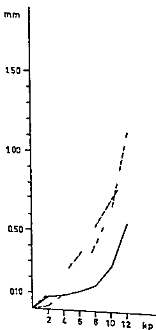


3pfix N (mod)

Exp 76



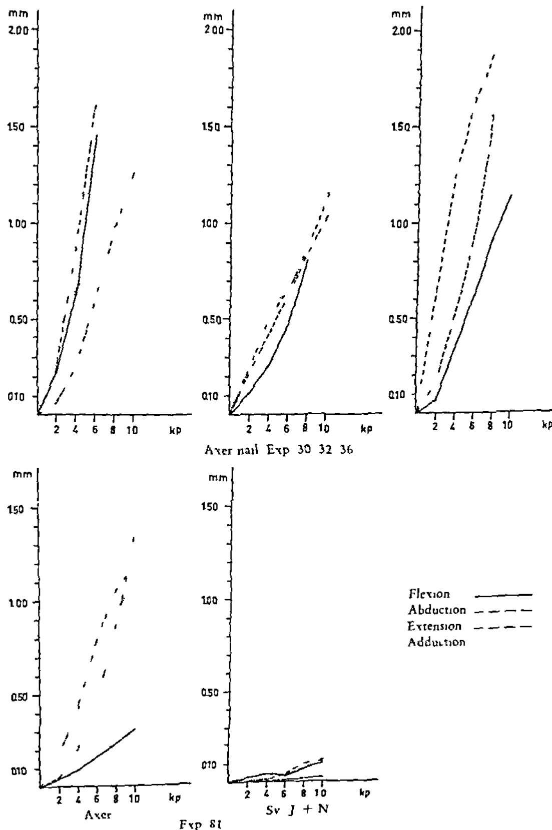
3pf x N

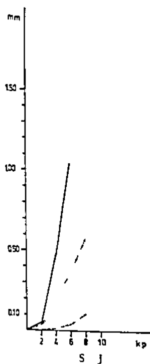


Mc Kee

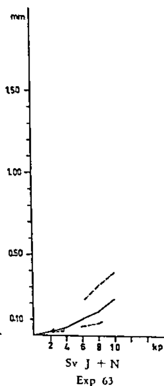
Exp 87

Fig 32 Examples of Loading Diagrams (S_{max} in mm as a function of loading)

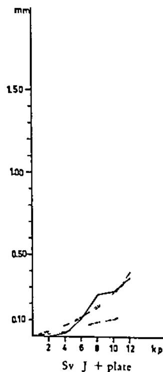




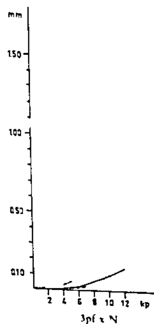
S J



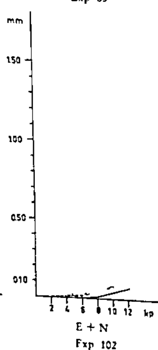
Sv J + N
Exp 63



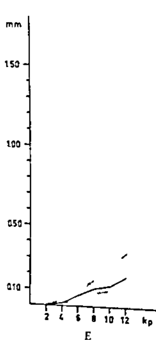
Sv J + plate



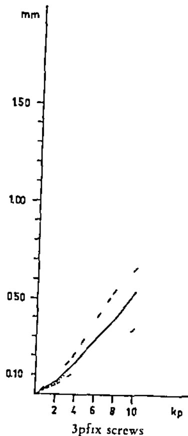
3pf x N



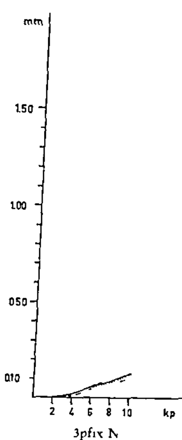
E + N
Exp 102



E

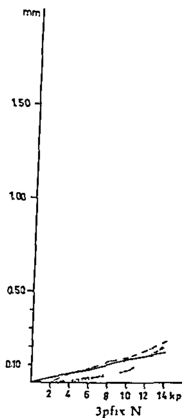


3pfix screws

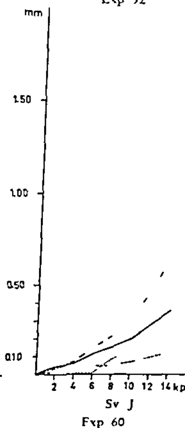


3pfix N

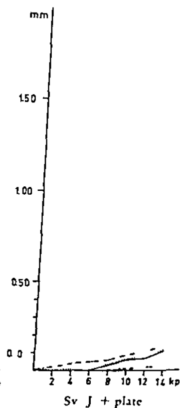
Exp 92



3pfix N



Sv J



Sv J + plate

Exp 60

General Summary

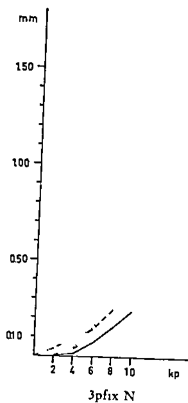
There are many methods described in the literature dealing with the operative technique of arthrodesis of the hip Certain problems have been of special interest The position of the arthrodesis the contact between the surfaces of the joint bone grafting additional subtrochanteric osteotomy and stabilization of the joint during the time of healing In the latter case the techniques recommended vary extremely However, the common opinion seems to be that some kind of osteosynthesis is necessary to obtain a successful result The attitude towards a plaster hip spica varies depending on how reliable the internal fixation is considered to be The evaluation of the stability of an osteosynthetic method is mainly based upon clinical observations

The opinions are thu not unanimous with respect to the elaboration of osteosynthesis in arthrodesis of the hip The aim with this study was to establish the extent of stabilization achieved by using various techniques of osteosynthesis and therefore experiments were carried out on autopsy specimens

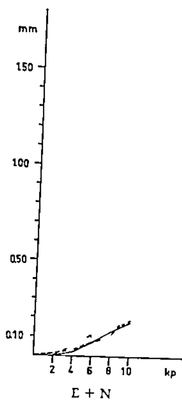
The simple nail reinforcement by the use of the three flanged nail was given special attention A theoretical analysis shows that in ideal conditions a minimum nail depth of 3 cm in the pelvis is necessary for satisfactory stabilization Furthermore it is essential that the nail be maximally secured to a cortical bone

The theoretical analysis served as a basis for an experimental study on the three-flanged nail Thus the nail was inserted into the acetabulum at varying depths and in different directions The nail was then subjected to bending moment and torque The resulting deflection was recorded

In comparing the values obtained in the theoretical analysis with those in the experimental investigation the latter values were higher In cases where the nail was inserted through an internal cortical layer the analytical and experimental values deviated more than when the nail was placed between the cortical layers The reasons are too small a nailing depth and fractures of the internal pelvic cortex These fractures cause a poorer connection of the bone around the nail The experiments revealed that a satisfactory result was obtained if the nail was inserted into the body of the iliac bone at a depth of approximately 4 cm Further depth of the



3pfix N



Σ + N

Exp 103

that the nails are placed at a maximum distance from each other at optimal angles to each other and can be inserted to the greatest depth

When testing the three flanged nail a marked impairment of the stability could be found at nail depths below 3 cm Therefore in the experiments where the three flanged nail was compared to the reference method only a greater nailing depth was accepted (mean value 4 4 cm) Even then the reference method was superior

In order to improve the stabilization with a three-flanged nail this nail was combined either with an N nail, or with a plate Two positions of the N nail were then compared An N nail directed in a lateral medial direction into the acetabular portion of the pubic bone was superior to one inserted in an anterior posterior direction into the bone area at the spina of the ischium At the continued experiments only the first mentioned position was therefore utilized In comparison with the reference method there was no significant difference The three flanged nail in combination with a sturdy metal plate which was attached to the iliac bone and the proximal end of the femur also gave results equal to the reference method

In an experimental series various types of compression nails were tried These were directed trans articularly into the pelvis and secured with a washer None of the tested methods resulted in the desired stability They were inferior to the reference method and even inferior to a three-flanged nail inserted at the recommended depth The reason of this probably was that the bone layer on the pelvic side penetrated by the compression nails did not have the necessary resistance The bone layer is too thin generally only about 15 mm and the cortex on the inside of the pelvis is weak

A comparison was also made between three point nail fixation and three point screw fixation the result of which was in the negative for the screw The screw is fit to resist axial tensile stress but of a corresponding nail dimension has a lower bending resistance and impaired ability to resist torque

Thus the results were equal between the reference method the three flanged nail and plate and the three flanged nail and N nail As the latter is easiest to apply there was reason to attempt improving on it The disadvantage of the method is connected with the traumatic effect of the nail The nail due to its design causes great resistance at the insertion This results in diastasis of the joint when the nail penetrates the acetabulum The bone layers which are passed may be fractured causing an impaired securing of the nail In an attempt to improve these deficiencies an experimental nail was designed By a special design of the tip of the nail and of the flanges the nail was easier to introduce and at the same time the risk of fissures occuring in the bone was diminished Due to the design of

nail only gave an insignificant increase in stabilization The nail then lay fixed between the cortical surfaces and could be regarded as secured to a *bone with cortical resistance properties In this* position, *the* securing in the pelvis was not inferior to that on the femoral side

Finally, these experiments also reveal that the three-flanged nail of the conventional type has a great tendency to causing fractures in the areas of bone through which it passes The greatest risk is the passage through the femoral head, as almost without exception fractures occur These appear as a fissure in the caput along the flange of the nail which is close to the surface or as a triangular fragment which is released These lesions are generally *not visible on the radiographs due to the opacity of the nail* and the conventional projection

A special measuring technique was elaborated in order to test the immediate stabilization obtained in autopsy specimens with various techniques of osteosynthesis in arthrodesis of the hip The calculations demand that the movement between the joint surfaces at the acetabular edge should be measured at three points, each in two directions Special extensometers were designed for this measuring The arising movement was transmitted by these extensometers to electric impulses which via an amplifier were recorded

The values obtained were concentrated to one value which represented the maximum movement The measurings were performed during gradually increased loading of the femur in four directions of mobility flexion abduction, extension and adduction By combining the values obtained for the maximum movement with the respective loads diagrams were plotted which represent the movement in the arthrodesis as a function of the loading

In several experimental series the various osteosynthetic methods were tried For statistical reasons it was considered justified to perform com*parative experiments on the same specimen As a reference method, osteo*synthesis with three Nystrom nails (N-nails) was selected The reason for this was that the N-nail did not damage the bone in such a way that the results of the subsequent osteosyntheses would *be affected negatively The* positions of the N nails were selected on the basis of an earlier investigation Thus one nail was inserted from a point below the greater trochanter upwards backwards into the body of the iliac bone The other was directed from the upper part of the greater trochanter in a horizontal direction into the acetabular portion of the pubic bone Finally the third was introduced from the front of the proximal part of the femur through the collum caput into the bone area at the spina of the ischium By applying the nails in these positions, the skeleton can be utilized to a maximum This means

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An electro-mechanic hammer was designed to futher reduce the risks of fractures when the nail was inserted The hammer allows an adjustment of both the *frequency of the strokes and the force of impact* Consequently, the insertion of the nail can be fully controlled

Conclusions

An experimental investigation was carried out on autopsy specimens for the assessment of the primary stability in arthrodesis of the hip The following conclusions can be made

Osteosynthesis with a trans-articular compression nail or a screw will give poor stabilization

Osteosynthesis with a three flanged nail will give a better stabilization provided that the nailing depth is at least 4 cm into the body of the iliac bone

Osteosynthesis with three Nystrom nails in described positions (three point fixation), three-flanged nail with a plate, and three flanged nail with one Nystrom nail in a described position will give good stabilization

Osteosynthesis using three-point fixation with screws will result in an inferior stabilization, as compared to three point fixation with nails of the corresponding dimensions

A very good stabilization was obtained with a new designed experimental nail in combination with one Nystrom nail in a described position These devices offer less difficulties at the application as compared to many others

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